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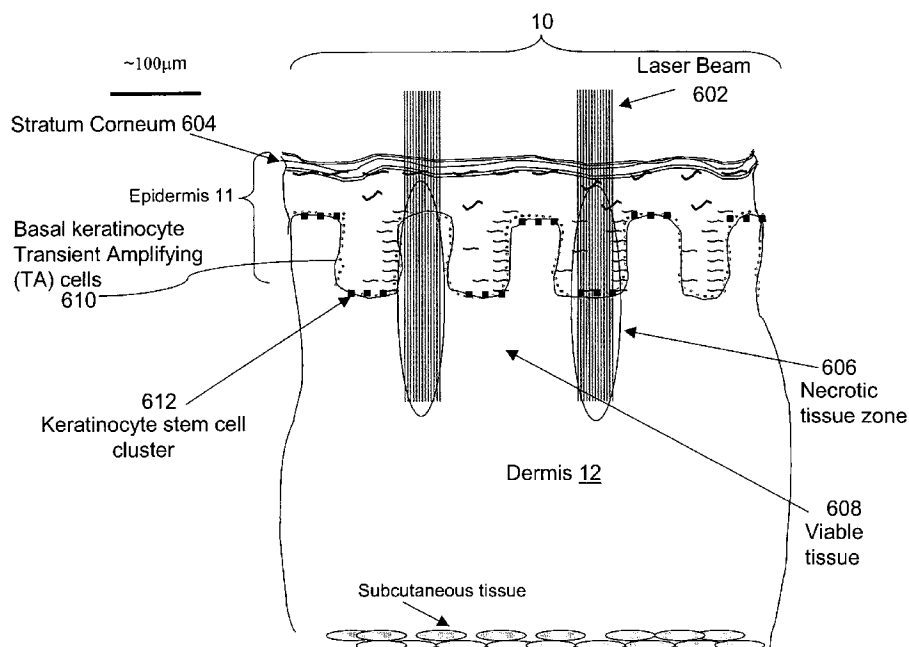
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(54) Title: METHOD AND APPARATUS FOR FRACTIONAL PHOTO THERAPY OF SKIN



(57) Abstract: A method and apparatus for providing fractional treatment of tissue (e.g., skin) using lasers is disclosed. The method involves creating one or more microscopic treatment zones of necrotic tissue and thermally-altered tissue and intentionally leaving viable tissue to surround the microscopic treatment zones. The dermatological apparatus includes one or more light sources and a delivery system to generate the microscopic treatment zones in a predetermined pattern. The microscopic treatment zones maybe confined to the epidermis, dermis or span the epidermal-dermal junction, and further the stratum comeum above the microscopic treatment zones may be spared.

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## METHOD AND APPARATUS FOR FRACTIONAL PHOTO THERAPY OF SKIN

### FIELD OF THE INVENTION

5 [0001] The present invention relates generally to methods and apparatus for providing medical or surgical treatment using optical energy, and in particular to a method and apparatus for providing fractional treatment of tissue (e.g., skin) using optical radiation.

### BACKGROUND OF THE INVENTION

10 [0002] Optical energy, particularly laser energy, is commonly used as a versatile tool in medicine to achieve desired outcomes in the tissue that is treated. For example, lasers have been used to treat common dermatological problems such as hypervascular lesions, pigmented lesions, acne scars, rosacea, hair removal, etc. Additionally, lasers are also used in aesthetic surgery for achieving better cosmetic appearance by resurfacing the skin and remodeling the different layers of skin to improve the appearance of wrinkled or aged skin. Generally, skin  
15 resurfacing is understood to be the process by which the top layers of the skin are completely removed by using chemicals, mechanical abrasion or lasers to promote the development of new, more youthful looking skin and stimulate the generation and growth of new skin. In laser skin remodeling, laser energy penetrates into the deeper layers of the skin and is aimed at stimulating the generation of and/or altering the structure of extra-cellular matrix materials,  
20 such as collagen, that contribute to the youthful appearance to skin. In traditional pulsed CO<sub>2</sub> laser resurfacing, the upper layers of skin may be completely ablated to a layer below the papillary dermis and there may be heat-diffusion-induced coagulation to several hundred micrometers below the original skin surface.

[0003] Generally, the desired effects on the skin are accomplished by laser-induced heating of  
25 the tissue. The induced heat results in thermal coagulation, cell necrosis, hemostasis, melting, welding, ablation and/or gross alteration of the extra-cellular matrix for specific temperature and heating time combinations. While using lasers for either skin resurfacing or remodeling, one of the important objectives has been to accomplish uniform treatment across the desired treatment area of the chosen skin site. Generally, particular care is exercised, either by the  
30 physician alone or by combining the physician's judgment with intelligence that is built into the dermatological system, to leave no tissue untreated in the targeted region of the skin. Whether one uses a broadly radiating pulsed beam of light or a focused laser that produces a relatively smaller spot size, the goal has been to expose the entire treatment area to the laser

energy, heat the entire volume of tissue in the treatment area and bring about the desired change. It has been widely reported that such broad area treatment results in undesirable side effects such as intolerable pain, prolonged erythema, swelling, occasional scarring, extended healing times and infection.

5 [0004] Erbium lasers and CO<sub>2</sub> lasers usually cause a thermal treatment to a well-controlled depth. In contrast, yellow pulsed dye lasers designed for selective photothermolysis of microvascular lesions cause selective thermal treatment of microvessels of varying depths (See generally, *Cutaneous Laser Surgery*, edited by MP Goldman and RE Fitzpatrick and published by Mosby, 1999). Depending on the kind of laser used (CO<sub>2</sub>, Erbium, etc.), the mode of usage  
10 (continuous wave or pulsed), the pulse width, energy density and power, different effects can be accomplished. **FIG. 1** illustrates the prior art treatment of ablative laser skin resurfacing, where the target tissue 10 is primarily the epidermis 11. Typical laser skin resurfacing using prior art systems completely ablates the targeted epidermis 11.

[0005] An approach used in treating microscopic pigmented tissue targets is to take advantage  
15 of the selectively absorbed pulse of radiation. Selective photothermolysis is accomplished by site-specific, thermally mediated injury of microscopic, pigmented tissue or a particular chromophore, where the selective absorption is due to the laser absorption characteristics of the pigmented tissue and/or the particular chromophore. For example, the laser wavelength is typically chosen to target hemoglobin or a pigmented chromophore, such as melanin.

20 [0006] Typically in these cases, whether it is skin resurfacing or selective photothermolysis of anatomical structures or defects that are located deeper in the skin, a burn or an acute wound is created by the laser. For acute wounds, the skin heals by three distinct 'response to injury' waves, as illustrated in **Fig. 2**. The initial inflammatory phase 202 has a duration lasting minutes to days and seamlessly transitions into the cell proliferative phase 204, lasting 1 to 14  
25 days. This cell proliferative phase is slowly replaced by the dermal maturation phase 206 that lasts from weeks to months (See, e.g., Clark, R. Mechanisms of cutaneous wound repair. In: Fitzpatrick TB, ed. *Dermatology in General Medicine*, 5<sup>th</sup> Ed., New York, NY. McGraw-Hill. 1999. pp. 327-41, which is incorporated herein by reference).

[0007] In general, a direct correlation exists between the size of the injury and the time  
30 required for complete repair. However, the inflammatory phase 202 is a function of cellular necrosis, particularly epidermal (i.e., keratinocyte) necrosis, and a direct correlation exists between cellular necrosis and the inflammatory phase. Increased cellular necrosis, particularly



epidermal necrosis, prolongs the inflammatory phase. Prolonging and/or accentuating the inflammatory phase may be undesirable from a clinical perspective due to increased pain and extended wound repair, and may retard subsequent phases of wound repair. The cause(s) of this prolonged inflammatory phase are not well understood. However, laser injuries are associated with early and high levels of dermal wound repair (e.g., angiogenesis, fibroblast proliferation and matrix metalloproteinase (MMP) expression) but delayed epidermal resurfacing (See, e.g., Schaffer et al., Comparisons of Wound Healing Among Excisional, Laser Created and Standard Thermal Burn in Porcine Wounds of Equal Depth, Wound Rep. Reg. v5 (1) pp. 51-61 1997, incorporated herein by reference). Unfortunately, most of the skin resurfacing efforts and selective photothermolysis treatments that affect large contiguous areas of chromophores result in a prolonged, exaggerated inflammatory phase leading to undesirable consequences such as delayed wound repair. The prolonged inflammatory phase also leads to the pain experienced by most patients undergoing skin resurfacing procedures. Undesirable extended inflammatory response phase can be attributed to the bulk heating of the skin with little or no healthy tissue, particularly keratinocytes, left behind in the area where the skin was exposed to the laser energy. Particularly when uniform treatment is desired and the entire target tissue volume is exposed to laser energy without sparing any tissue within the target volume, pain, swelling, fluid loss, prolonged reepithelialization and other side effects of dermatological laser treatments are commonly experienced by patients.

[0008] Many systems have been devised to minimize epidermal necrosis. One such approach includes cooling the epidermal surface using plastic bags filled with ice placed on the skin surface for a short while (about five minutes), compressed freon gas used during irradiation, or chilled water spread directly on the area being irradiated. Some of these methods are described in, for example, A. J. Welch et al., "Evaluation of Cooling Techniques for the Protection of the Epidermis During ND-YAG Laser Irradiation of the Skin," Neodymium-YAG Laser in Medicine, (Stephen N. Joffe ed. 1983). Various devices and approaches have been proposed to treat dermal tissue regions without damaging the epidermal regions. One approach to minimize bulk heating of the skin is described in U.S. Pat. No. 6,120,497. In this approach for treating skin wrinkles, the dermal region is targeted in order to elicit a healing response to produce unwrinkled skin, and the epidermal region above the targeted dermal region is simultaneously cooled. In another example, U.S. Pat. No. 5,814,040 describes cooling an epidermal tissue region while performing selective photothermolysis of selected buried chromophores in biological tissues using a laser. This cooling procedure is known as dynamic cooling. As illustrated in Fig. 3, an epidermal tissue region is cooled by spraying a cryogen

302 on the surface of the epidermis 11 to establish a predetermined dynamic temperature profile. The epidermal 11 and underlying dermal 12 tissue regions are subsequently irradiated (not shown) to thermally treat the dermal tissue region (i.e. the altered tissue region 304) while leaving the epidermal tissue region substantially undamaged.

- 5 [0009] Another approach to sparing the epithelium during laser procedures includes a laser system that delivers laser energy over a relatively large tissue surface area with the laser light focused in the dermis (See, e.g., Muccini et al., "Laser Treatment of Solar Elastosis with Epithelial Preservation," *Lasers Surg. Med.* 23:121-127, 1998). In this system, air is used as the coolant to maintain reduced temperature at the skin surface. Additionally, the optical  
10 device focusing the laser light also acts as a thermal conductor on the surface to help minimize surface temperature as air is flowed over the optical device to keep it cool.

- [0010] All of these systems pose practical limitations because of the complexity added by the cooling system. Hence, there is a need for an improvement in the art for a system and method to treat the dermal region and avoid the complexities associated with cooling. In addition, all  
15 of these systems are macroscopic in nature, i.e., they expose the entire skin surface within the treatment region to laser irradiation (bulk heating) and cooling. These global treatments lead to an increase in clinical side effects and to an increase in healing time as described above. Hence, there is a need for an improvement in the art for a system and method to treat the dermal and epidermal regions that reduce the side effects associated with global non-ablative  
20 as well as ablative treatments. This reduction in side effects will allow physicians to increase the treatment intensity so that skin treatments can be provided more effectively.

- [0011] When lasers act on the skin to cut, vaporize or coagulate tissue there are several 'zones' of tissue damage that surround the spot where the impact of the laser energy is the highest, i.e., the treatment zone where the tissue volume is necrosed either completely or to a level above a  
25 threshold, such as about 90% or more of the cells being necrosed. These zones are illustrated in **FIG. 4**. Usually, the temperature in the necrotic zone 402 has reached a value greater than about 70°C, and the tissue, whether it is made up primarily of cells, keratinocytes and their derivatives or collagen, is necrosed or denatured, respectively. The center of the necrotic zone is typically close to the center of the treatment beam. For heating times on the order of about  
30 1-10 milliseconds, cell necrosis, coagulation and protein denaturation will occur in a range of or above about 65-75°C. Immediately adjacent to the area of necrosis is a thin thermal coagulation zone of tissue clumping (not shown), where denatured proteins have formed an area that contains necrotic cells, matrix, and cellular debris. Surrounding this zone is a larger

zone of thermally-altered but viable tissue or a Heat-Shock Zone (HSZ) 404 in which proteins and cells have been heated to supra-physiologic temperatures over a short time, but a significant percentage still remain viable. In portions of this HSZ, the volume of the tissue is exposed to temperature typically in the 37°C to 45°C range – a range in which approximately 100% of the cells survive the treatment. The dimensions of these zones depend on various laser parameters (such as, wavelength, pulse duration, energy density, etc.), thermal and optical properties of the tissue components, and ambient temperature. Recent data indicate that the HSZ has special significance for subsequent biologic effects (See, e.g., Capon A. and Mordon S. Can thermal lasers promote wound healing? *Am. J. Clin. Dermatol.* 4(1):1-12. 2003, which is incorporated herein by reference). For illustrative purposes, the demarcation between the different zones is shown as an abrupt change. However, one skilled in the art would understand that the change from one zone to another is not abrupt, but gradual. Outside of the thermally-altered/HSZ 404, essentially unaltered healthy tissue 406 exists. Necrotic zone 402 and surrounding HSZ 404 together form a volume of thermally-altered tissue 408. Temperatures in the tissue above about 100°C may cause steam to form in the tissue, which may cause disruptive effects.

[0012] Heat shock in the thermally-altered zone 404 triggers multiple signaling pathways that induce both cell survival and programmed cell death. The final outcome as to whether a cell lives or dies is believed to depend on the ‘acquired stress tolerance’ of the surrounding tissue. Mild heat shock followed by a period of recovery makes cells more resistant to subsequent severe heat shock and multiple other stresses. This is achieved via the activation of cell survival pathways (i.e., extracellular signal-regulated kinase, ERK, and akt kinase) and the inhibition of apoptotic pathways (i.e., Jun terminal kinase, Fas, caspase-8 and others) via heat shock protein (i.e., HSP72) mediated signaling events (See, e.g., Gagai VL and Sherman MY, Interplay between molecular chaperones and signaling pathways in survival of heat shock. *J. Appl. Physiol.* 92:1743-48. 2002, which is incorporated herein by reference).

[0013] In conventional skin resurfacing and selective photothermolysis of contiguous chromophore regions, the laser exposed tissue is dominated by the necrotic treatment zone instead of the viable, heat shock zone. In fact, such conventional treatments are designed to cover the target tissue in the plane of the skin completely with overlapping necrotic zones so that no target tissue is left unexposed to laser energy. In contrast to conventional treatments, to promote the cell survival pathways and inhibit the apoptotic pathways, it is desirable to have the viable tissue be more prevalent in the laser exposed tissue compared to the necrotic zone.

There is an unmet need for a laser treatment that enhances the proportion of a viable tissue portion in the target tissue volume.

## SUMMARY OF THE INVENTION

**[0014]** In general, the present invention features a method for treating either existing medical (e.g., dermatological) disease conditions or for improving the appearance of tissue (e.g., skin) by intentionally generating a pattern of thermally altered tissue surrounded by unaltered tissue. The thermally altered tissue may include a necrotic zone. This approach offers numerous advantages over existing approaches in terms of safety and efficacy. This invention minimizes the undesirable side effects of pain, erythema, swelling, fluid loss, prolonged reepithelialization, infection, and blistering generally associated with laser skin resurfacing. Another aspect of this invention is to stimulate the tissue's wound repair system, by sparing healthy tissue around the thermally altered tissue, whereby the repair process is more robust. Yet another distinguishing feature of this invention is to reduce or eliminate the side effects of repeated laser treatment to tissue by controlling the extent of tissue necrosis due to laser exposure.

**[0015]** One aspect of the present invention is a method for achieving beneficial effects in a target biological tissue comprising treating the target tissue using optical radiation to create one or more "microscopic" treatment zones such that the aspect ratio of the necrotic zone width to the necrotic zone depth is above about 1:2, preferably above about 1:4, and the treatment zones are created by a predetermined treatment pattern. Another aspect of this invention is a method for achieving beneficial effects in skin tissue comprising treating the skin by exposing a targeted part of the skin tissue to optical radiation to create one or more microscopic treatment zones such that the volume of the target tissue that remains unaffected by the optical radiation is controlled, and further that the ratio of the sum of the treatment zone volumes to the target tissue volume is less than one.

**[0016]** In one aspect of the invention, the microscopic treatment zones are created by using lasers with wavelengths in the range of 0.4 to 12.0  $\mu\text{m}$ , directing the laser radiation to a targeted region in the skin, and creating microscopic treatment zones of necrotic tissue. These microscopic treatment zones could be in the epidermal or dermal regions or originate in the epidermal region and continue into the dermal region of the skin. In some embodiments, the upper layers of the epidermis, such as the stratum corneum, are spared and left substantially intact. The individual microscopic zones could have the shape of a cylinder, sphere, or any

other shape that could be generated by an appropriate combination of wavelength, pulse duration, pulse width, beam profile, pulse intensity, contact tip temperature, contact tip thermal conductivity, contact lotion, numerical aperture of the focusing elements, optical source brightness, and power. Individual microscopic treatment zones are generally columnar in shape, which is beneficial for healing purposes. The microscopic treatment zones could be between 10 and 4,000  $\mu\text{m}$  in the propagation direction of the beam (depth) and between 10 and 1,000  $\mu\text{m}$  in the direction perpendicular to the beam (diameter).

[0017] Another specific aspect of this invention is a method of creating the microscopic treatment zones of necrosed tissue that allows viable tissue to be interspersed between the microscopic treatment zones thereby enabling the skin to mount a more robust repair response.

[0018] This invention also relates to an apparatus for treating common medical conditions by treating a target tissue volume in the skin with optical energy and creating one or more necrotic zones such that the aspect ratio of the necrotic zone diameter to the necrotic zone depth is at least about 1:2, and the necrotic zones are created by a predetermined treatment pattern.

Another aspect of this invention relates to an apparatus that exposes a targeted part of the tissue to optical radiation to create one or more thermally altered treatment zones such that the volume of the target tissue that remains unaltered by the optical radiation is controlled. Further, the ratio of the sum of the thermally altered zone volumes to the target tissue volume is less than or equal to one.

[0019] Yet another aspect of this invention is an apparatus that provides the predetermined treatment pattern comprising at least one source of optical radiation and a delivery system operably coupled to the source and configured to direct the optical radiation to a volume of tissue in a predetermined pattern. The predetermined treatment pattern comprises a plurality of discrete microscopic treatment zones, wherein a subset of the plurality of microscopic treatment zones include individual discrete microscopic zones comprising necrotic tissue volumes having an aspect ratio of at least about 1:2. The source of radiation may include one or more lasers, flashlamps or LEDs. The delivery system may include various optical systems and/or scanner systems, such as lens arrays and galvanometer-based scanners, respectively.

## BRIEF DESCRIPTION OF THE DRAWINGS

[0020] These and other features, objects and advantages of the present invention are more readily understood from the following detailed description in conjunction with the accompanying drawings, where:

5 [0021] FIG. 1 is an illustration of skin exposed to laser radiation using a prior art system for skin resurfacing.

[0022] FIG. 2 is a schematic showing the inflammatory, cell proliferative, and dermal maturation phase of normal cutaneous wound healing.

10 [0023] FIG. 3 is an illustration of skin exposed to laser radiation using a prior art system for skin remodeling.

[0024] FIG. 4 is a schematic showing the different zones in a piece of skin exposed to laser radiation and consequent heat treatment.

[0025] FIG. 5 is an illustration of laser resurfacing using a prior art system.

[0026] FIG. 6 is an illustration of embodiments of the present invention.

15 [0027] FIGS. 7, 8 and 9 are schematics of the different thermally altered zones created by the incorporation of this invention.

[0028] FIGS. 10 and 11 illustrate different embodiments of this invention.

[0029] FIGS. 12a-12h illustrate various microscopic treatment zone shapes in accordance with various embodiments of the invention.

20 [0030] FIGS. 13a-13c and 14a-14g are graphical representations of different thermally altered zones created by various embodiments of the invention.

[0031] FIG. 15 is a schematic illustrating an embodiment of an apparatus for practicing the invention.

[0032] FIG. 16 shows an embodiment of the control system of the inventive apparatus.

25 [0033] FIG. 17 shows an embodiment of the optical system of the inventive apparatus.

[0034] FIG. 18 shows an embodiment of the delivery system of the inventive apparatus.

[0035] FIG. 19 is an illustration of a method of using of the inventive apparatus.

[0036] FIGS. 20, 21a, 21b and 22-24 are embodiments of systems for practicing the present invention.

- 5 [0037] FIGS. 25a and 25b show histological results from laser treatments applied utilizing embodiments of the present invention.

### DETAILED DESCRIPTION

[0038] Embodiments of the present invention provide a method and apparatus to increase the safety and efficacy of treating biological tissue with optical radiation, including dermatological  
10 treatments using lasers. Particularly, different embodiments of the present invention may be suitable to treat a variety of dermatological condition such as hypervascular lesions including port wine stains, capillary hemangiomas, cherry angiomas, venous lakes, poikiloderma of Civatte, angiokeratomas, spider angiomas, facial telangiectasias, telangiectatic leg veins; pigmented lesions including lentigines, ephelides, nevus of Ito, nevus of Ota, Hori's macules,  
15 keratoses pilaris; acne scars, epidermal nevus, Bowen's disease, actinic keratoses, actinic cheilitis, oral florid papillomatosis, seborrheic keratoses, syringomas, trichoepitheliomas, trichilemmomas, xanthelasma, apocrine hidrocystoma, verruca, adenoma sebaceum, angiokeratomas, angiolymphoid hyperplasia, pearly penile papules, venous lakes, rosacea, wrinkles, etc. Embodiments of the present invention may be used to remodel tissue (for  
20 example, for collagen remodeling) and/or to resurface the tissue. While specific examples of dermatological conditions are mentioned above, it is contemplated that embodiments of the present invention can be used to treat virtually any type of dermatological condition. Additionally, embodiments of the present invention may be applied to other medical specialties besides dermatology. Other biological tissues may be treated with embodiments of  
25 the present invention, and in particular tissues with structures similar to human skin may be treated. For example, tissues that have an epithelium and underlying structural tissues, such as the soft palate, may be treated using embodiments of the present invention. Skin is used in many places in this application as an example of one biological tissue that has been treated using embodiments of the present invention. However, it should be understood that the  
30 invention is not limited to skin or dermatology alone.

[0039] A primary mechanism of the present invention is the sparing of volumes of tissue within a larger tissue treatment area. In other words, leaving healthy tissue between and around necrotic treatment zones and HSZs has a number of beneficial effects that are exploited by various embodiments of the present invention. If the HSZs surrounding adjacent necrotic treatment zones are appropriately spaced and/or epidermal injury is limited, the viable tissue bordering thermal coagulation zones will be subjected to less inflammation from the products of cell death, thereby favoring cell survival over apoptosis. These areas will be better able to mount reepithelialization and fibro-proliferative and subsequent remodeling phases of wound repair. One important reason for this effect is that HSZs and bordering spared tissue contain subpopulations of stem cells responsible for repopulating the epidermis (See, e.g., Watt F, "The Stem Cell Compartment in Human Interfollicular Epidermis", J Derm. Sci., 28, 173-180, 2002, which is incorporated herein by reference). In humans, stem cells reside in two locations in the skin: 1) in focal clusters of the basal keratinocyte layer, in contact with basement membrane components and, 2) in the follicular bulge area of the pilosebaceous unit. The basal keratinocyte layer of the epidermis typically contains a low population of these stem cells interspersed with large numbers of transit-amplifying (TA) cells that are directly derived from stem cells. Interfollicular epidermal stem cells tend to cluster at the bases of rete ridges in acral areas and at the tips of dermal papillae in non-acral skin. The follicular stem cell compartment has been shown to possess the ability to repopulate the interfollicular epidermal surfaces when required under certain conditions. Such conditions include severe burns, large split-thickness epidermal injuries and cosmetic surgical procedures (e.g., ablative laser resurfacing, chemical peel, dermabrasion, keratotomy, etc.) that denude the epidermal layer, leaving no epidermal stem cell populations. Such denuding of the epidermal layer is illustrated in **FIG. 5** by the large size of the laser beam treating a large area of the epidermis. In fact, it is well known that CO<sub>2</sub> resurfacing results in prolonged reepithelialization when compared to steel scalpel or electrosurgical scalpel incisions even though laser wounds exhibit accelerated dermal healing (See, e.g., Schaffer et al., Comparisons of Wound Healing Among Excisional, Laser Created and Standard Thermal Burn in Porcine Wounds of Equal Depth, Wound Rep. Reg. v5 (1) pp. 51-61 1997, which is incorporated herein by reference). Reepithelization to repair such defects is delayed under these circumstances, because healing must occur from remaining follicular stem cell populations within the de-epidermized wound and from epithelial stem cells at the margins of the defect. If the wound is full thickness, extending down to the level of the pilosebaceous unit, then healing is delayed even further because epidermal healing occurs only from the margins.



[0040] The speed of epidermal reepitheliazation is directly proportional to the number and density of TA and stem cells. In the case of the follicular stem cell population, the average density of the bulge area compartment is dependent on the number of pilosebaceous units per unit of skin surface area. For the densest hair bearing skin (scalp) the number of adult human hair ranges between 100 and 500 per  $\text{cm}^2$ ; whereas surfaces such as the face have less than half that density. On the face, at least a two or three orders of magnitude greater density of epidermal stem cells exists versus follicular bulge stem cells based on the density of epidermal stem cell clusters that reside in the basal cell layer immediately above each dermal papilla in non-acral skin, where they are spaced every 10-100  $\mu\text{m}$ .

[0041] Fractional laser treatments according to embodiments of the present invention are illustrated in **FIG. 6**. If the entire volume of the target tissue is not treated but only a fraction of the tissue is treated by laser beams 602 thereby permitting the existence of viable tissue 608 (which typically includes HSZs and untreated, healthy tissue) between necrotic tissue zones 606, with multiple treatments, macroscopic areas of tissue regeneration will occur at the maximum rate within the surrounding micro-HSZs and spared epidermal surfaces, creating a 'fractional wound repair field' within the target treatment area 10. Such treatment may further include, but is not required to include, sparing the outermost layers of the epidermis, for example the stratum corneum, from significant damage. Such sparing of the stratum corneum promotes healing by maintaining the structural integrity and protective character of the stratum corneum. Fractional wound repair fields are fundamentally different from previous techniques because the areas of epidermal tissue that are spared between necrotic zones contain both epidermal stem cells 612 and TA cell populations 610. Thus, re-epithelization of necrotic zones proceeds rapidly with few or none of the side effects (i.e., pain, persistent erythema, edema, fluid drainage, etc.) observed after traditional resurfacing procedures. A small necrotic zone cross-section (e.g., less than about 250 microns in diameter for a circular cross-section) means that a significant number of stem cells and TA cells are relatively close to the center of the treatment zone throughout the depth of the treatment zone. This further speeds the healing response, such that substantially complete (e.g., greater than about 75% complete) re-epitheliazation typically occurs in less than about 36 hours post-treatment for necrotic zone cross-section widths in a range less than about 250 microns, and preferably for cross-sectional widths less than about 100 microns substantially complete re-epitheliazation occurs less than about 24 hours post-treatment. Re-epitheliazation typically occurs at a rate directly proportional to the cross-sectional width of the necrotic zone. As a further example, if the spacing between fractional beam treatment zones creates an average density (i.e. number of

necrotic zones per unit surface area of the target treatment area 10) of 500 necrotic zones/cm<sup>2</sup> there are ample epidermal stem cells that remain for interfollicular resurfacing of both the necrotic zone itself and of the surrounding HSZs, if necessary. In addition, after fractional laser treatment, the follicular bulge stem cell population remains intact, so they may participate in wound healing and resurfacing, as needed. The density of treatment may alternately be described with a fill factor (i.e. surface area receiving radiation or necrosed divided by total surface area of the target treatment area 10), wherein a typical fill factor for embodiments herein may be between about 0.05 and about 0.95, and preferably between about 0.1 and about 0.5.

10 [0042] Chronic UV irradiation appears to trigger dysfunctional wound repair pathways in the skin that involve gradual replacement of normal epidermal and dermal structures with characteristic atrophy and accumulation of elastotic dermal matrix components (See, e.g., Kligman, "Prevention and Repair of Photoaging: Sunscreens and Retinoids", *Cutis*. 1989 May;43(5):458-65). Currently, reversal of photo-aging is attempted by imparting cutaneous injury that induces new dermal collagen formation. Such cutaneous injury could be accomplished using mechanical (e.g., dermabrasion), chemical (e.g., retinoids and acid peels), or laser surgical procedures. The expectation is that these cutaneous injuries will promote the normal fibro-proliferative responses of the upper reticular and papillary dermal compartments, and therefore yield rejuvenated skin. For example, U.S. Pat. No. 6,120,497 describes thermally injuring collagen in the targeted dermal region to activate fibroblasts. The fibroblasts in turn deposit increased amounts of extracellular matrix constituents. However, as discussed above with reference to **Fig. 2**, epidermal injury promotes the inflammatory phase, which inhibits the rejuvenative process. As can be easily imagined, dermabrasion, which is a mechanical surface ablation process, results in epidermal injury. Hence, while the currently used methods, which are mentioned above, for promoting normal fibro-proliferative response of the dermal compartments can yield rejuvenated skin, due to the epidermal injury that occurs with these processes, the rejuvenative process is compromised.

30 [0043] An objective of nonablative photorejuvenation is to induce a thermal wound repair response in the papillary and upper reticular dermal compartments (approximately 100-400  $\mu$ m below the surface of the skin) while sparing the epidermal compartment. To spare the epidermis, one typically uses low fluences (laser energy densities). Unfortunately, such low levels are generally inadequate to promote the kinds of stimulation that are required to cause the desired dermal effect. Thus, prior art approaches result in minimal efficacy. In most cases,

minimal dermal matrix remodeling and minimal clinical responses (e.g., wrinkle reduction, retexturing, dyschromia reduction, and telangiectasia removal) are achieved by these procedures (See, e.g., Nelson et al., "What is Nonablative Photorejuvenation of Human Skin", Seminars in Cutaneous Medicine and Surgery, Vol. 21, No. 4 (Dec.), 238-250, 2002; Leffell D, "Clinical Efficacy of Devices of Nonablative Photorejuvenation", Arch. Dermatol. 138: 1503-1508, 2002). Therefore, there is an unmet need for sparing the epidermal compartment, but achieving enough stimulation of dermal matrix remodeling to be clinically effective.

**[0044]** By creating isolated, non-contiguous (i.e. discrete) treatment zones having necrotic tissue surrounded by zones of viable (i.e. heat altered viable tissue and often untreated, unaltered healthy tissue) tissue that are capable of promoting healing, the present invention induces multiple sites of tissue regeneration to produce 'micro-thermal wound repair fields'. We call this process fractional photo therapy, as fractional volumes of the target tissue volume are thermally altered, as opposed to the conventional treatments where the entire target volume is thermally altered or damaged. Each field is typically composed of thousands of individual thermally altered zones (i.e. HSZs and surrounding spared tissue units) that comprise "nodes" of wound repair. The healing mechanisms (e.g., stem cells and TA cells) of each node can be expected to expand beyond the volume of the node to merge with neighboring nodes, replace photo-aged tissue components (e.g., solar elastosis, microvascular ectasia, pigment incontinence, epidermal atrophy, and atypia), and produce complete coverage. Hence, there is a need for generating isolated, non-contiguous tissue volumes having treatment zones composed of necrotic tissue, surrounded by zones of viable tissue that are capable of promoting healing of the target tissue. The present invention meets this need.

**[0045]** Furthermore, some embodiments of the present invention protect the stratum corneum and uppermost layers of the epidermis from ablation, puncture or other significant damage. This is typically achieved by such means as choosing appropriate pulse energies and durations, and using a contact window placed against the tissue during treatment. For example, sapphire or diamond windows may be used for their high thermal conductivity and transparency to pertinent wavelengths. Additionally, choosing wavelengths that act on water as the primary or substantially only chromophore assists in limiting damage to the stratum corneum, as the stratum corneum typically includes relatively small amounts of water. The result of these embodiments is to maintain the integrity of the stratum corneum such that its physical structure is intact. This allows the stratum corneum to continue its normal function of protecting tissue underneath it from infection, dehydration, etc. For most tissue, water makes up a large part of

the tissue such that water as a chromophore is typically contiguous throughout the treatment volume. In such tissue for embodiments using water as the primary chromophore, selective photothermolysis typically has little application, and it is the beam shape and parameters that define necrotic zones and that allow viable tissue to remain between necrotic zones. Contact windows are not required for all embodiments of the present invention. Non-contact windows may be used, such as, for example, windows set at a constant height above the tissue surface. Further, contact windows may be less than 100% transparent to the treatment beam wavelength, such as, for example, less than about 75% transparent. Additionally, contact windows may have low thermal conductivity. Such partially transparent and/or low thermal conducting contact windows may beneficially generate heat for use as part of a treatment.

[0046] FIGS. 6 through 9 illustrate some embodiments of this invention. In FIGS. 6 through 9, target tissue 10 is the volume of tissue comprising thermally altered and unaltered tissue that is being addressed by the therapy. In FIGS. 6 and 7 the intended treatment is resurfacing of the skin so that the patient's skin looks younger and healthier. The objective is to remove a portion of the epidermis 11 and stimulate the rejuvenation process in the dermal region 12. As shown in FIG. 4, the thermally altered volume of tissue 408, comprises the treatment zone 402 and the HSZ 404. The thermally unaltered tissue 406 surrounds the thermally altered volume of tissue 408. The thermally altered volume of tissue 408 comprising the treatment zone 402 and the heat shock zone 404 (HSZ) is further illustrated in FIGS. 7 through 9. For illustrative purposes the boundaries between the treatment zone 402 and the HSZ 404 are clearly marked. One skilled in the art would understand that the treatment zone 402 is made up of tissue that has been almost completely necrosed (e.g., such that greater than about 75%, and preferably greater than about 90%, of the originally viable cells in the zone are necrosed post-treatment) and the HSZ 404 is made up of substantially viable tissue that has been thermally altered (e.g., such that greater than about 50% of the cells in the zone that were viable before treatment are still viable). Treatment zone 402 is made up of tissue that has lost its inherent biological activity and has typically experienced temperatures higher than about 70°C for a significant length of time (i.e. greater than about 1 millisecond). HSZ 404 is the tissue volume surrounding necrotic zone 402, and HSZ 404 has typically been exposed to temperatures above 37°C and up to as much as 55°C-65°C, for typical heat exposure times of about 1 msec or less. This thermally altered tissue is viable and capable of mounting and assisting a robust tissue repair response. One skilled in the art understands that the boundary regions are not clearly defined in that there is typically a temperature gradient from the center of the necrotic zone outward, such that heating and the percentage of cell necrosis decreases from the necrotic zone

402 through the HSZ 404. The necrosis process is typically described by an Arrhenius-type model where thermal damage is cumulative, irreversible and linked to the time of exposure and heating rate.

5 [0047] FIG. 7 illustrates the situation where the necrotic zones 402 are predominantly in the epidermis 11, with viable tissue 704 between necrotic zones. FIG. 6 illustrates the effect of the inventive treatment where a significant portion of the keratinocyte stem cell cluster 612 and the basal keratinocyte transient amplifying cells 610 are spared. Again, one skilled in the art would understand that the treatment zones 402 and the HSZs 404 do not abruptly end at the epidermal-dermal junction, but are substantially in the dermis as well. It is likely that there  
10 will be a thermal spread into the dermis 12. The extent of the thermal spread is generally a function of the power, pulse width, repetition rate for multiple laser firings, and wavelength of the laser beam, the numerical aperture and focus depth of the optical system, and the thermal conductivity and temperature of the tip that could be placed in contact with the surface of the skin, all within the context of the scattering, absorption and thermal conductivity  
15 characteristics of the tissue.

[0048] FIG. 8 illustrates a skin remodeling treatment where the target tissue 10 is the primarily in the dermis 12. Thermally altered tissue 802 is primarily confined to the dermis 12. Again, it is to be understood that it is likely that a thermal spread could occur in the epidermis 11.

20 [0049] FIG. 9 shows where the thermally altered tissue 902 spans the epidermis 11 and the dermis 12. This illustrates the situation where one desires to have skin resurfacing, partial removal of the epidermis 11, and collagen shrinkage in the dermis 12. Additionally, Fig. 9 illustrates sparing the stratum corneum at the tissue surface in area 906.

[0050] FIG. 10 shows an alternate embodiment of the present invention, where the heat shock zones 1004 overlap. The center of the target zones 1002 are separated by pitch 1006. If the  
25 pitch is less than the diameter of the HSZs 1004 then the HSZs overlap. These overlapping HSZs 1004 can be positioned such that, overall, the target tissue 10 is left with no thermally unaltered tissue. One way the HSZs 1004 can be made to overlap with each other is by adjusting where the laser beam lays down the spots (i.e. where the center of the necrotic zones 1002 are placed). For example, if two spots are within less than about 100 microns of each  
30 other, there will typically be such overlap. If two or more treatment zones 1002 are designed to lie in close proximity to each other and if the spots are laid down in quick succession, then the net increase of temperature due to closely spaced treatment zones may be sufficient to

increase the size of individual HSZs **1004**. In this type of treatment, it is important for the treatment zones that are contributing to the creation of the HSZs to be created in a time short enough to prevent thermal diffusion from removing thermal energy from the adjacent treatment regions that are contributing thermal energy to the creation of the spatially enhanced HSZ. Another method uses a combination of thermal diffusion and overlap of thermal energy to create spatially enhanced HSZs. It should be noted that the thermal diffusion constant depends on the chemical constituents of the tissue (i.e. bone, fat, tendon, etc.), dimensions of the cell structures, water content and heat dissipating blood flow. Consequently, the thermal diffusion constants are different in the avascular epidermis and highly vascularized dermis.

An alternative way to overlap the HSZs **1004** will be to make the HSZ **1004** significantly larger than the treatment zone **1002**. One approach to make the HSZ **1004** larger than the treatment zone **1002** is to generate the desired treatment zone **1002** using high energy densities, such that high temperature regions are created. These high temperature zones would then spread the thermal energy over a larger volume that would result in a larger HSZ **1004**. It may be detrimental to various treatments to have the treatments zones so close that they overlap, as this may cause blistering and/or significant clefting or lift-off at the dermal-epidermal junction.

[0051] As illustrated in **Fig. 11**, one important aspect of this invention is skin laser treatment that intentionally leaves behind healthy, substantially unaltered tissue **1102**, such that the substantially unaltered tissue **1102** helps in skin remodeling and wound repair of the treatment zones **1104**. **Fig. 11** depicts target tissue **10** made up of necrotic zone **1104**, HSZs **1106**, and thermally unaltered tissue **1102**. Thermally unaltered tissue **1102** typically does not receive any laser light directly from the treatment system. Laser light from the treatment system typically radiates the tissue surface only within necrotic zone **1104**. As described in further detail below, the shape and size of the treatment zone **1104** and the consequent HSZ **1106** can be controlled by choosing the appropriate laser parameters. The volume of the unaltered tissue **1102** and the spacing between zones of thermally affected tissue **1104** and **1106**, and thermally unaltered tissue **1102** can also be controlled by choosing the appropriate treatment parameters and treatment beam spacing. Additionally, the stratum corneum may be protected and maintained intact, or it may be ablated or damaged during treatment, depending on the desired effect. In various embodiments described below, necrotic zones and HSZs may be created in a predetermined pattern (e.g., a polygonal grid pattern, a circular pattern, a spiral pattern, a dot matrix, dashed lines, dashes, lines, etc.) or in a random pattern. If a predetermined pattern is used, the pattern may be uniform, non-uniform or partially uniform in shape and/or spacing,

and the individual treatment volumes may be substantially uniform, substantially non-uniform or partially uniform in shape and size. Within a larger treatment area, subsets of necrotic zones and HSZs may be overlapping to create clusters or lines of necrotic zones, with areas of healthy tissue between clusters or lines (e.g., dashed lines less than about 1 centimeter).

- 5 Additionally, different embodiments may include the use of treatment beams of optical radiation that are interleaved or sequentially, simultaneously or randomly generated to create the predetermined or random patterns.

### **Controlling the shape and depth of the treatment zones**

- 10 [0052] A wide variety of treatment zones of varying depths and shapes can be created using the optical systems described herein. The shape of the region of necrosis created in the tissue, and the shape of the HSZ surrounding it can be adjusted using appropriate combinations of the laser parameters.

- 15 [0053] The shape of the treatment zones is affected by a combination of the wavelength of the light, the size and shape of the optical beam, the optical focusing, the flatness of the skin surface and the laser pulse parameters (e.g., energy, duration, frequency). The wavelength of the light selects values for the optical absorption strength of various components within the tissue and the scattering strength of the tissue. These optical transport parameters determine where the light energy travels in the tissue, and serve to partially determine the spatial temperature profile in the tissue. The size and shape of the optical beam and the focusing or numerical aperture of the laser determines gross propagation properties of the beam inside the tissue. Size (e.g., diameter for a circular beam shape or cross-sectional width for a polygonal or irregularly shaped beam) and shape of the optical beam, particularly as the optical beam enters the tissue, typically affects the shape of the resulting necrotic zone. For example, a polygonal cross-section for the optical beam may produce a polygonal columnar necrotic zone, and a circular optical beam cross-section typically produces a circular or oval necrotic zone cross-section. Cross-sectional width for beam shape means the smallest distance across the cross-section in a line that includes the center of the cross-section. Cross-sectional width includes diameter, as diameter is simply a specific instance for a circular beam cross-section. Focusing, or numerical aperture (N.A.), is a significant factor for determining the ratio of the surface temperature of the tissue to the peak temperature reached in the most intensely affected zone. Embodiments of the present invention may include varying or alternating focal depths for one or more optical beams impacting a give treatment zone. For example, such embodiments may include multiple optical beams focused to different depths, or the may
- 20
- 25
- 30

include a single beam that is focused to varying depths within a treatment zone. The magnitude of the temperature profile is determined in part by the laser pulse energy.

[0054] The shape and size of a treatment zone is roughly determined by the region of the tissue that reaches a temperature in the appropriate temperature range for that treatment. Thus, for example, a particular treatment may be divided up into zones A-D. For example, zone A might be the region where the peak temperature reaches 75°C or higher, zone B might be the region where the peak temperature lies in the range 62-75°C, zone C might be the region where the peak temperature lies on the range 45-62°C, and zone D might be the region where the peak temperature lies below 45°C. These temperature ranges may be set by a practitioner of the present invention to define regions where particular desirable (or undesirable) effects are dominant in the tissue, according to the earlier description of the influence of heat on human tissue. Typically, for temperatures above about 70°C for heating durations of greater than about 1-2 msec, tissue will coagulate and necrose and proteins will be denatured. Heat shock zones will typically be created for tissue temperatures less than about 45-50°C. One of ordinary skill will recognize (a) that more or fewer zones may be defined with different temperature ranges in characterizing the 'fractional' aspects of this invention, and (b) that the definition of a treatment zone may be based on tissue biochemistry rather than on the peak temperature. For example, an area having cell necrosis to a level of greater than about 75%, and preferably greater than about 90%, of all cells being necrosed is considered herein as a necrotic zone. Necrosis may be determined by a variety of histological processes, including for example, hematoxylin and eosin (H & E) stains or nitro-blue tetrazolium chloride, a lactate hydrogenase (LDH) activity stain. Loss of birefringence due to thermal denaturation of collagen may be evaluated, for example, using cross-polarized light microscopy.

[0055] An example of the control of heat affected zones using the laser pulse energy is provided by the case of a collimated or weakly diverging incident laser beam. In this situation, the beam spreads out inside the tissue, and creates treatment zones that resemble concentric shells centered on the point of entry of the laser into the skin. The 'treatment' in each of these treatment zones is defined by the temperature range achieved in the specific zone. In the absence of skin surface cooling, the zones may well extend out to the skin surface and indeed in this case some part of the skin surface usually lies in the most intensely affected zone (i.e. the zone with the highest temperature rise). If the laser pulse energy is small, these zones do not penetrate deeply into the skin. For weak laser pulse energy, only the least intense treatment zones (e.g. zones C and D of the previous paragraph) will be created. The zones for



the more intense treatments do not exist for weak laser power. For higher laser pulse energy the treatment zones penetrate more deeply into the skin, and zones of increasing treatment levels (e.g. zone B and then A of the previous paragraph) are created close to the surface. As the laser energy is increased further the smaller zones close to the surface expand to greater depths in the skin.

[0056] A further example of the control of thermally altered zones (and especially necrotic zones) using the laser power and wavelength and external focusing is provided by the case of a tightly focused incident laser beam. In this situation, the effective beam diameter tends to reduce inside the tissue, reaching its smallest diameter (effective "focus") at a depth given by the balance between focusing and optical scattering. At levels deeper than the actual focus the beam spreads out rapidly. In the wavelength region around 1450 nm, the absorption depends strongly on the wavelength. For this example, we select the wavelength so that the absorption depth is equal to the depth of the actual focus. Further, the focal length of the incident laser beam is selected so that the on-axis intensity of the laser beam increases for increasing depth below the tissue surface, peaks at or near the actual focus, and then decreases.

[0057] Under these circumstances in this example, the following beneficial result is obtained – the necrotic zones, as well as typically the surrounding HSZs, are substantially columnar regions or columnar shells centered about the actual focus. By substantially columnar we mean a shape that is approximately cylindrically symmetric along the optical axis of the treatment and deeper into the tissue than it is wide. It includes shapes such as spheroidal (round-ish), ellipsoidal (fat cylinder), cylindrical (right cylinder), bispherical (pinched cylinder), or conoid (tapered). Other words to describe the columnar shape might be cigar-like, prolate-, right-cylindrical, or conical. Substantially columnar as used herein includes circular (e.g., Fig. 12a (1202)), oval or elongated (e.g., Fig. 12b (1208)), irregular (e.g., Fig. 12d (1220)) or polygonal (e.g., Fig. 12c (1214)) shaped cross-sections (i.e., cross-sections perpendicular to the optical axis of the treatment beam). As illustrated in Fig. 12g, the cross-section may also be annular in shape, such that the necrotic zone 1240 surrounds a viable tissue portion 1242. Substantially columnar necrotic treatment zones are further described as elongated in the direction parallel to the optical axis of treatment. Substantially columnar further includes necrotic zones with sides or lateral aspects that are substantially parallel to the optical axis of treatment, although this includes sides that are up to about 40° tilted (e.g., angle 1230 in Fig. 12e or angle 1238 in Fig. 12f) in either direction with respect to the optical axis of treatment. The term substantially columnar does not necessarily imply symmetry below and

above the actual focus, and further includes sides that are bulged or indented. For example it includes a shape which is a half-spheroid above the actual focus and a tapered conoid below the actual focus.

5 [0058] At low laser pulse energy, only one zone is created, that is, the zone corresponding to the weakest treatment (e.g. Zones D or C). For the parameters given in this example, this shape will be substantially columnar. For larger pulse energy, the zones are longer and a little wider. At still larger pulse energy, the new zones corresponding to more intense treatments appear as small regions centered on the actual focus. At still larger pulse energy, the zones all increase in size. And so on, until at the highest laser pulse energies, the most intensely  
10 affected zone created is a zone corresponding to over-treatment (e.g., charring and/or ablation) of the tissue.

[0059] In each of these examples the temperature history of the tissue is typically relevant. For short laser pulses, where heat transport is not strong during irradiation, the temperature at any location in the tissue rises to its peak value, (thus determining the zone type for that  
15 location), and then decays back to ambient temperature as a result of heat transport. The rate at which the temperature decays depends on several factors, including the water content of the tissue, the degree of vascularization of the tissue, the physical size and shape of the treatment zones and the actual temperature profile in the tissue. There is evidence that the rate of rise of the temperature can significantly affect the response of the tissue to the increased temperature.  
20 A rapid rise may cause a more intense reaction than a slow rise. Also a previously treated region may respond differently from a previously untreated region. To the extent that the actual temperature history is significant, the laser pulse length can be adjusted to control this parameter. For reproducible results, a preferred embodiment selects a pulse length for which the effects of a slow temperature rise or possible thermal pre-treatment are avoided.  
25 Separation between thermally-altered zones avoids adjacent treatment zone heating. This is generally achieved for shorter pulse lengths (i.e. less than about 25 msec) for necrotic zone cross-sectional widths less than about 150 microns. However, this recommendation for the pulse length should not be construed as a limitation on the invention.

[0060] The optical properties of the tissue may vary with temperature and biochemistry. For  
30 example it is well-known that optical absorption features in the skin are known to vary with temperature. Also, optical scattering in the dermis is believed to decrease and then increase with increasing thermal denaturation of collagen. The use of all these effects by adapting the

laser parameters to account for them and take advantage of them is within the scope of the present invention.

[0061] This type of control has been verified using computer modeling and also by experiments on human tissue. Based on this modeling and experiments, it is possible to set the laser irradiation parameters to achieve either or both of epidermal treatment and deeper dermal treatment. For collimated or diverging incident beams the shell zones lie close to the skin surface and often touch it, and for tightly focused incident beams, columnar zones can be centered well below the skin surface. In particular, the shape of the treatment zones can be varied among all the shapes described above, by adjusting one or more various parameters such as the wavelength, external focus power (in diopters) or numerical aperture, external pressure on the skin, the presence or absence of a contact plate at the skin surface, the laser pulse energy and laser pulse duration, laser beam shape and size, and the repetition frequency of pulses. Some embodiments take advantage of the temperature-based shifts of the absorption features in skin to control precisely the shape and extent of the treatment zones.

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### **Modeling Guidance**

[0062] We provide here a model for use in practicing this invention. The general shape of the heated region is approximated by a model in which the RMS radius of the heated region as a function of t and z is

$$\rho^2 = (R^2 - w^2)(z/f - 1)^2 + w^2 + b^2 z^3 + 4Dt$$

20

where z is the depth below the surface, t is time since the optical pulse began, R is the radius of the beam at the skin surface, f and w are the location and size, respectively, of the beam waist in the absence of scattering. Scattering and thermal diffusion are represented by the last two terms, where  $b^2 = 1/3 \mu(1 - \langle \cos\theta \rangle)$ , and D is the thermal diffusivity within the tissue.  $\mu$  is the scattering coefficient,  $\theta$  is the scattering angle, and  $\langle \cos\theta \rangle$  is the average value of the cosine of the scattering angle. Within this model the temperature rise in the tissue at the end of the laser pulse as a function of r is

25

$$T = \frac{\alpha E e^{-\alpha z}}{C \pi \rho^2} e^{-(r/\rho)^2}$$

where  $\alpha$  is the optical absorption of the tissue,  $E$  is the laser pulse energy that enters the skin,  $C$  is the specific heat of the skin, and  $\rho$  is evaluated at the end of the optical pulse where  $t = \tau$ . Within this model, the boundaries between treatment zones may be based on the magnitude of the temperature at the end of the pulse.

- 5 [0063] Along the optical axis of the beam (i.e.,  $r=0$ ), the temperature profile is determined by the competition between reduced beam diameter in tissue and optical absorption. The actual focus of the beam, where the beam waist  $\rho$  is smallest, typically occurs at a depth  $z_0$  less than  $f$ , as a result of scattering. The actual beam waist is  $w_0 = \rho(z_0)$  evaluated at the beginning of the optical pulse, where  $t=0$ . For weak absorption, the temperature is highest at depth  $z_0$ , whereas  
 10 for strong absorption the heated region lies closer to the skin surface. There is therefore an absorption value for which the temperature rise below the skin surface is a maximum. It is given by

$$\alpha_{peak-T} z_0 = 1$$

[0064] The ratio of the temperature rise at the surface to the temperature rise at depth  $z$  is

15 
$$\frac{T(0)}{T(z)} = e^{-\alpha z} \left( \frac{\rho(z)}{R} \right)^2 \approx \frac{w^2 + b^2 z_0^3}{e R^2}$$

Given  $z_0$ , these equations indicate the optimal absorption and the beam parameters to use to select a suitable surface temperature rise. The wavelength is chosen to achieve a desired absorption based on target chromophore(s), whereas the relation between  $z_0$  and the focal length  $f$  depends on the scattering, which the practitioner generally has minimal ability to  
 20 control.

[0065] The shape of the treatment zones may be described by the location of the boundaries between treatment zones. Within this model, they are given by  $T(r,z) = \text{constant}$ .

$$\left( \frac{r}{w_0} \right)^2 = \left( \frac{\rho}{w_0} \right)^2 \left[ K^2 - \alpha(z - z_0) - 2 \ln \left( \frac{\rho}{w_0} \right) \right]$$

- where  $K$  is a constant such that the radius of the treatment zone boundary at  $z = z_0$  is  $K w_0$ .  
 25 Note that whether the depth of interest  $z$  is deeper or shallower than the actual focus, the ratio  $\rho/w_0$  is always greater than one.  $\rho/w_0$  is therefore quadratic in  $z-z_0$  near the actual focus, but

may increase faster than this at greater distances from  $z_0$ . The boundaries predicted in this way are substantially columnar in the sense described above.

[0066] One of ordinary skill will recognize many of the assumptions that underlie the model. This model is informed by more detailed calculations involving optical refraction and diffraction, Monte Carlo light propagation and thermal diffusion in three spatial dimensions, and detailed reaction rates for biochemical processes in tissue. We therefore offer this model as a general guide to the practitioner of the invention in selecting appropriate parameters for the control of the various treatment zones.

[0067] After the optical pulse has terminated, the heat in the tissue continues to diffuse and raise the temperature of the surrounding tissue. There is usually more thermal energy in a treatment zone (e.g., necrotic zone or thermally altered zone) than the minimum required to raise the temperature of the tissue to the level to achieve the particular tissue condition for that zone. This extra energy is available to cause further tissue changes in the surrounding regions. Thermal diffusion and other known mechanisms cause this transport to occur. Thermal diffusion therefore has the effect of expanding the treatment zone by an amount that depends on its excess thermal energy and the radius of the lesion. The net effect of thermal diffusion is that it expands the treatment zone and tends to make the treatment zones more spherical. The effect is generally small unless very large amounts of excess energy are applied to the tissue or the lesion has a large diameter.

[0068] One important aspect of thermal diffusion that is evident in **Figs. 13** and **14** is that the temperature gradients are favorable for heat transport of heat deeper into the tissue than the laser light itself penetrates. Thermal diffusion may add up to 200 microns or more to the depth of a treatment zone as a result of this longitudinal heat transport.

[0069] Representative results using the model are presented in **Figs. 13a-13c** which illustrate the range of treatment zones achievable by adjusting the focusing strength of the beam incident on the surface. The various contour lines on the graphs indicate contours of constant temperature. These representative results are consistent with typical treatment results using embodiments of the present invention on humans.

[0070] For example, **Fig. 13a** illustrates the type of zone boundaries that are predicted by this model. The parameters were set to the following:  $\mu = 100/\text{cm}$ ,  $\theta = 100 \text{ mrad}$ ,  $R = 1\text{mm}$ ,  $w = 50 \mu\text{m}$ ,  $f = 500 \mu\text{m}$ , and  $\alpha = 20/\text{cm}$ . The actual focus is at  $z_0 = 495 \mu\text{m}$ , and the actual beam

waist is 81  $\mu\text{m}$ . This corresponds to tight focusing to a point 500 microns below the tissue surface.

[0071] In Fig. 13b, the parameters are set to the following:  $\mu = 100/\text{cm}$ ,  $\theta = 100 \text{ mrad}$ ,  $R = 1 \text{ mm}$ ,  $w = 500 \mu\text{m}$ ,  $f = 500 \mu\text{m}$ , and  $\alpha = 20/\text{cm}$ . The actual focus is at  $z_0 = 495 \mu\text{m}$ , and the actual beam waist is 504  $\mu\text{m}$ . This corresponds to weak focusing of the beam to a point 500 microns below the tissue surface.

[0072] In Fig. 13c, the parameters are set to the following:  $\mu = 100/\text{cm}$ ,  $\theta = 100 \text{ mrad}$ ,  $R = 1 \text{ mm}$ ,  $w = 950 \mu\text{m}$ ,  $f = 500 \mu\text{m}$ , and  $\alpha = 20/\text{cm}$ . This corresponds to using a collimated incident beam.

[0073] FIGS. 14A, 14B, 14C, 14D, 14E, 14F and 14G further illustrate different shapes in the thermally altered tissue (i.e. necrotic zone 21 and HSZ 22) caused by embodiments of the present invention. For example, the treatment parameters that are used to produce the treatment zone in FIG. 14A result in a necrotic zone 21 that has its largest diameter in the epidermis, with a HSZ 22 that is approximately 200  $\mu\text{m}$  in diameter. A different set of treatment parameters is used to produce the necrotic zone in FIG. 14D. These parameters result in a necrotic zone that penetrates significantly deeper into the skin and has a significantly smaller radius within the top 100  $\mu\text{m}$  of the skin. In addition, these parameters result in a HSZ 22 that is significantly wider and deeper than the corresponding HSZ of FIG. 14A. The shape of the treatment zone will dictate to a large extent the shape of the HSZ, as a HSZ is generated in part by thermal diffusion of the heat energy deposited in the necrotic zone. The shape of the necrotic zone can be controlled by the appropriate combination of one or more of the laser beam spot size, fluence (energy per unit area), pulse duration, energy per pulse, laser wavelength, optical beam profile, system optics, lotion, contact tip temperature, surface cooling, and contact tip thermal conductivity.

[0074] For example, a circular laser beam of 1500 nm wavelength emitted from a single mode fiber, focused to a depth of 615  $\mu\text{m}$  within the skin with a pulse energy of 12 mJ, an exposure time of 12 ms, a peak power of 1 W, an optical magnification of approximately 6:1 (i.e., the image is 6 times smaller at the focal point in comparison with the object at the output of the fiber when focused in air instead of in skin), and a passively cooled glass plate in contact with the skin through an optically transparent index matching lotion will create a necrotic zone 21 that is approximately cylindrical as shown in FIG. 14D. Cross sections of several such necrotic regions 21 are shown in FIGS. 14A, 14B, 14C, 14D, 14E, 14F and 14G. For this type

of treatment, the resulting necrotic zone 21 will be approximately 100 to 300  $\mu\text{m}$  in diameter (perpendicular to the direction of the incident beam) and approximately 150 to 900  $\mu\text{m}$  deep in the direction of the beam. FIGS. 14A, 14B, 14C, 14D, 14E, 14F and 14G further illustrate the shape and depth of the thermally altered zones 22 that may be created by various combinations of laser pulse duration, pulse energy, and focal depth. In these figures, the y axis shows the depth of penetration of the thermally altered zone from the surface of the skin, where 0 is the skin surface and -600 would indicate 600  $\mu\text{m}$  into the skin. The x axis shows the size of the altered tissue zone in the radial direction. FIGS. 14A, 14B, 14C, 14E, 14F and 14G show shapes of the treatment zone 21 and the HSZ 22 that may be generated by using the same parameters as used for FIG. 14D, but with changes in the pulse duration, pulse energy, and focus depth as described in Table 1. As can be seen by examining FIG. 14C, necrotic zones can be created that are non-cylindrical.

TABLE 1:

|          | Pulse Duration<br>(msec) | Pulse Energy<br>(mJ) | Focus Depth Below The<br>Surface Of The Skin ( $\mu\text{m}$ ) |
|----------|--------------------------|----------------------|--|
| FIG. 14A | 3                        | 3                    | 55   |
| FIG. 14B | 12                       | 12                   | 55   |
| FIG. 14C | 12                       | 12                   | 335  |
| FIG. 14D | 12                       | 12                   | 615  |
| FIG. 14E | 20                       | 20                   | 615  |
| FIG. 14F | 12                       | 12                   | 755  |
| FIG. 14G | 25                       | 25                   | 755  |

[0075] Typical aspect ratios for treatments using embodiments of the present invention should typically be greater than about 1:2 (or 1-to-2), and preferably greater than about 1:4. For example, an aspect ratio of 1:2 would mean that for every 1 micron of diameter of the necrotic zone, there is 2 microns of depth of the necrotic zone. Aspect ratio is the cross-sectional width (e.g., diameter for circular cross-sections) of the necrotic zone (i.e. typically at its widest point

in a direction perpendicular the optical axis of the treatment beam) divided by the total depth of the necrotic zone measured along the optical axis of treatment of the optical radiation.

Cross-sectional width is measured across the largest cross-sectional area of the necrotic zone, and the cross-sectional width is the smallest distance across the cross-sectional area along a

5 line that includes the center of the cross-sectional area. Depth is measured from the top of the necrotic zone to the bottom of the necrotic zone along the optical axis of the optical radiation. For example, Fig. 12h illustrates an example of an elliptical cross-sectional area 1244, and the cross-sectional width is the minor axis 1246. An aspect ratio can be defined similarly to include the diameter and depth of the HSZ.

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### **Embodiments and Examples**

[0076] One embodiment of the apparatus used for practicing this invention is shown in FIG.

15 15. Apparatus 1500 comprises a control system 1530, an optical radiation source 1510, and a delivery system 1520 to deliver the desired pre-determined treatment pattern to the target tissue 10. The control system 1530 is operably connected to the optical radiation source 1510 and the delivery system 1520. The control system 1530 may include separate control systems (not shown) for the optical system and the delivery system. For certain applications, the optical radiation source 1510 includes multiple laser light sources, which can be arranged in an array, such as a one-dimensional array or a two-dimensional array.

20 [0077] FIG. 16 shows a block diagram of the control system 1530. Control system 1530 is operably connected to the input/output 1602, the optical source 1604, the scanning element 1606, the optical element 1608 and the sensing element 1610. Input/Output 1602 could be a touch screen element or other such means that are well known in the art. The sensing element 1610 may include an optical, mechanical or electrical sensor or detector, such as, for example, an optical mouse, a mechanical mouse, capacitance sensor array or profilometer.

25 [0078] FIG. 17 shows an embodiment in which the optical source 1710 includes laser light sources 1740 arranged in a one-dimensional array 1720. A laser light source can provide one or more optical beams having particular optical parameters, such as optical fluence, power, timing, pulse duration, inter-pulse duration, wavelength(s), and so forth, to produce a desired dermatological effect in the target tissue 10. The wavelength is typically chosen largely based on target chromophore whether naturally found in the skin, such as, for example, water, hemoglobin or melanin, or added to the skin via topical or injection, such as, for example, drugs incorporating or attached to a chromophore. By way of example, a laser light source can

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provide an optical beam having a wavelength or range of wavelengths between approximately 400 nm and 12,000 nm, such as between approximately 500 nm and 3,000 nm, or preferably between about 1000 nm and about 2000 nm, or more preferably between about 1400 nm and about 1600 nm. For example, for purposes of non-ablative coagulation of a dermal layer of the targeted portion **10**, a laser light source can provide an optical beam having a wavelength of approximately 1,500 nm and an optical fluence incident on the outer surface of the skin between approximately 0.001 Joules/cm<sup>2</sup> and 100,000 Joules/cm<sup>2</sup>, such as between approximately 1 Joules/cm<sup>2</sup> and 1000 Joules/cm<sup>2</sup>. The energy would typically be in a range less than about 100 mJ per pulse, with a pulse duration less than about 100 msec. For certain applications, the pulse duration of an optical beam can be approximately equal to or less than a thermal diffusion time constant, which is approximately proportional to the square of the diameter of a focal spot within the targeted portion, associated with the desired treatment zone. Pulse durations that are longer than the thermal diffusion time constant can be less efficient and cause the focal spot to expand or shrink undesirably by thermal diffusion. This is one approach for making HSZs **1004** overlap, as shown in FIG. **10**.

[0079] Examples of optical radiation sources include, but are not limited to, diode lasers, diode-pumped solid state lasers, Er:YAG lasers, Nd:YAG lasers, Er:glass lasers, argon-ion lasers, He-Ne lasers, carbon dioxide lasers, excimer lasers, fiber lasers, such as erbium fiber lasers, ruby lasers, frequency multiplied lasers, Raman-shifted lasers, optically-pumped semiconductor lasers (OPSL), and so forth. For certain embodiments, a laser light source is desirably a diode laser, such as an infrared diode laser. The optical radiation sources may be continuous wave (CW) or pulsed. However, it should be recognized that the selection of a particular type of laser light source in the optical system is dependent on the types of dermatological conditions to be treated using the dermatological apparatus **1500**. In Fig. **17**, the optical radiation source **1710** could include one particular type of laser light source capable of providing one wavelength or wavelength range. Alternatively, the optical source **1710** could include two or more different types of laser light sources to provide a variety of different wavelengths or wavelength ranges. Optical beams from different laser light sources can be directed to the targeted portion **10** on a one-by-one basis or at the same time. In addition, one skilled in the art will recognize that while laser sources are the preferred embodiment of the optical source described here, other optical sources such as a flashlamp, an optical parametric oscillator (OPO) or light-emitting diode could also be used.

[0080] Referring to FIG. 18 as another embodiment, the optical delivery system 1830 also includes an optical element 1808 that is optically coupled to the optical source (not shown). The optical element 1808 has a numerical aperture greater than about 0.005, can be either a collimator or a focusing element and functions to direct optical energy from the optical source to the targeted portion 10. In the present embodiment, the optical element 1808 directs optical energy to the targeted portion 10 by focusing the power of the optical energy to one or more treatment zones 1802 within the target tissue 10. Desirably, multiple treatment zones are simultaneously or sequentially exposed to optical energy. Multiple treatment zones can be separated from one another so as to form discrete treatment zones. Alternatively, or in conjunction, multiple treatment zones can intersect or overlap one another.

[0081] In the present embodiment, the optical element 1808, in conjunction with the delivery system, directs optical energy in a pattern, such as a discontinuous or microscopic pattern, so that one or more treatment zones are exposed to optical energy sequentially or simultaneously. Use of a pattern of optical energy provides greater efficacy of treatment by allowing for control of the fraction of the target tissue 10 that is exposed to optical energy. Different patterns can provide a variety of different thermally altered zones and a particular pattern can be selected based on the type of dermatological condition to be treated. For instance, in the case of a sensitive dermatological condition such as dermal melasma or deep pigmented lesions, the use of a pattern of optical energy permits an effective level of treatment within multiple treatment zones. At the same time, by controlling the fraction of the targeted portion 10 that is exposed to optical energy, pain, immune system reaction, trauma, and other complications can be reduced. By having the treatment zones adjacent to healthy and substantially undamaged cells, healing of the targeted portion 10 is quicker, since the possibility of congestion or impairment of repair processes is reduced. Use of a pattern of optical energy also can facilitate multiple treatments to produce a desired effect by allowing safer individual fractional treatments to be combined to produce a significant result. This is typically milder and poses a lower risk to the patient. Furthermore, visible impressions of treatment can be reduced by using a pattern of treatment where an individual treatment zone is on the same or smaller scale than the normal visible texture or constituents of the skin itself. Such reduced visible impressions may mean that the necrotic zones are sub-surface or have surface cross-section dimensions less than about the size of skin pores. Such reduced visible impressions may mean that individual necrotic zones are substantially not visible to the naked human eye observing from 3 feet or more away from the skin surface. Predetermined patterns may be chosen based on the effect desired in the tissue. Such patterns may be uniform or non-uniform, as may the individual

treatment zones. Predetermined patterns may include polygonal grids, circular patterns, spiral patterns and others. Such patterns may be formed using one or more optical sources irradiating in a sequential, random pattern or interleaved firing mode. The resulting pattern may alternately be random.

- 5    **[0082]** Fig. 19 illustrates another embodiment in which a hand-piece 1910 is sized and configured to be used by an operator in treating a patient's skin according to various embodiments of the present invention. The hand-piece is operably coupled to the control unit 1920.

#### **Selection of Parameters**

- 10   **[0083]** In accordance with the inventions disclosed herein, for treatments near the surface of the tissue, there is great latitude in the selection of irradiation parameters, as the heat-affected zones can be limited to a small region by focusing of the light, or by other means such as optical interference.

- 15   **[0084]** For deeper treatments, the benefits of the present invention are obtained using any one of a number of combinations of parameters for the irradiation system, as outlined herein based in part on the above model. With respect to the irradiation source, the wavelength may be adjusted to optimize both the tissue absorption and scattering. For example, to achieve treatment zones centered at a depth of 1mm, the absorption coefficient should be about 10/cm, if scattering is low, and less than this for deeper treatments.

- 20   **[0085]** The absorption in human tissue in the visible light range is mostly due to specific chromophores (such as hemoglobin or melanin) and scattering is generally too strong to meet the conditions given herein for deeper treatment zones. In the near-infrared radiation range, water is typically the only, or vastly the most significant, chromophore. The absorption coefficient for water in the near infrared range has peaks near 1450 nm (i.e. absorption  
25   coefficient of about 30/cm) and 1950 nm (i.e. absorption coefficient of about 200/cm) and between these peaks it does not drop significantly below 10/cm. Above the peak at 1950 nm the absorption does not drop to small values but increases to extremely high values comparable to the absorption of Er:YAG laser light and/or CO<sub>2</sub> laser light. Between 1000 nm and 1450 nm the absorption coefficient rises steadily, and can be as low as 2/cm or less. Below about  
30   1000nm, chromophores such as hemoglobin and melanin become more prevalent, and water absorption recedes. Thus, in the wavelength region between 1000 nm and 2000 nm, the absorption of skin is in the range suitable for efficient treatments to depths of a few mm or

less. In this wavelength range, the scattering strength (i.e. the scattering constant) of skin is about 100 /cm but is peaked forward so that the effective extinction rate by scattering is substantially reduced, and in fact weak enough to allow significant penetration of focused light to a few millimeters depth, without excessive spreading of the light energy. This combination  
5 of relatively weak absorption and scattering in this wavelength range is attractive for the formation of columnar treatment zones at depths up to a few mm.

[0086] The laser power should be adjusted so that there is just enough optical energy introduced into the skin to create the desired necrotic zones and HSZ zones. An excess of energy will create larger zones than desired, whereas a lack of adequate energy may fail to  
10 create the desired zone at all. There is greater latitude in the pulse length of the optical pulse. The pulse length should be chosen long enough to avoid excessive intensity at the skin surface, but short enough to avoid significant heat transport during the pulse. For a zone of dimension  $L$ , the pulse length is proportional to  $L^2/D$ , and optimizes at about  $L^2/4D$ , where  $D$  is the effective diffusion coefficient. This typically amounts to about 1ms for a zone size of 100  
15 microns. Longer pulse widths will create larger treatment zones and will require greater pulse energy than the minimum required. In this regard, Q-switching may cause undesirable tissue damage, but if high intensity is desirable, then Q-switched laser systems may be used to advantage in obtaining fractional treatments, especially for treatment zones within 100 microns of the skin surface.

[0087] Yet another means for controlling the treatment zones is to use more than one light  
20 source. Such sources may be directed through the same aperture to the skin, or through separate apertures. They may be applied simultaneously or sequentially, or interleaved in any way. Each source creates its own temperature profile, so that the actual temperature profile is the sum of all the individual profiles. Thus, a band of wavelengths, such as is provided by  
25 some diode lasers, will create treatment zones that are elongated columnar zones. Use of two wavelengths may create a treatment zone that is a combination of a deeper and a shallower zone, and so on. Moreover, frequency chirped pulses may also be used in this way. One of ordinary skill will recognize the potential for further fine adjustment of the shape and depth of the treatment zones using multiple sources of different wavelengths or directed through  
30 different apertures to the skin surface with appropriate temporal sequencing.

[0088] Embodiments of the present invention wherein pulses are interleaved provide treatments where a response of the tissue to one wavelength conditions the tissue for an enhanced response at another. For example, a first treatment beam is applied having a given

wavelength, pulse duration, energy and beam diameter calculated to heat the tissue. A second treatment beam is then applied to coagulate the heated tissue starting at the higher base temperature caused by the first treatment beam. Alternately, a first treatment beam may target one chromophore, while the second treatment beam targets a second different chromophore.

5 [0089] It will also be evident to one of ordinary skill that there are many optical means of directing light to the skin surface in order to create a desired pattern of energy at or below the skin surface. These include, but are in no way limited to, lenses, mirrors, beam splitters, fiber optics, diffraction gratings, diffractive elements and holographic elements. Any and all such means are within the scope of the inventions disclosed herein in that they may be used,  
10 individually or in combination with each other, to create a pattern of irradiation and thereby control the shape of the treatment zones. In particular, any means of creating a substantially columnar treatment zone is within the scope of this invention.

[0090] Another aspect of this invention is the arrangement of the individual treatment zones such that healthy, un-treated tissue is left between zones of heat-affected or treated tissue.  
15 Means of creating a pattern of individual treatment zones include, but are not limited to, fly's eye lenses, acousto-optic and electro-optic deflectors, diffractive elements, galvanometers, piezo-electric devices, MEMS, and rotating scanning elements. Scanner technology is well-developed and may be applied to this function. One embodiment employing scanner technology includes a device wherein the scanning function is included in a hand-piece or head  
20 which moves slowly over the tissue surface, while applying many optical pulses that each create an individual treatment zone. The separation between the treatment zones is a critical parameter for fractional treatments and is best accomplished using technology that controls the pattern of irradiation sites precisely. However, the motion of optical parts within the head, coupled with the finite pulse width of each individual pulse, causes the optical pulse to sweep, or blur, over a small but finite path during irradiation. Such blurring can be controlled by  
25 making the pulse length short, or by slowing the motion of the moving optical components, or by active control of the blurring process (i.e. de-blurring). The first two options have the consequence of limiting the area of the patient's skin that can be covered per unit time. However, de-blurring of the irradiation pattern enables a greater area of skin to be treated per  
30 unit time. Accordingly the de-blurring function lies within the scope of our invention to the extent that it keeps the individual treatment zones sharp, yet enables a rapid scan over the patient's skin treatment area. Typically such a rapid scan includes moving a handpiece or a delivery system portion at up to about 10 centimeters per second. An embodiment including

such de-blurring is found in co-pending U.S. Patent Application No. 10/750,790, filed on December 31, 2003, which is incorporated herein by reference.

### **Alternate Embodiments**

[0091] As will be evident to one of ordinary skill in the art, there are many possible configurations of laser sources, optics and hardware that provide a means of controlling the shape, location and pattern of the treatment zones according to our invention. The following embodiments and examples represent varying degrees of sophistication in implementing means of creating treatment zones in human tissue using the teachings provided herein.

[0092] One embodiment of the invention is to utilize a compact diode laser or a fiber laser as a source of optical energy. The source is located conveniently near the patient, and the light energy is transported to the immediate vicinity of the treatment area using optical fibers. In general, the optical energy emerging from the optical fiber has some, but not all of the characteristics of the light that are required by the tissue treatment being performed. The fiber terminates in a hand-piece that is held by the practitioner over the treatment area. The function of the hand piece is to perform a local and final conditioning of the optical energy to have the correct parameters as described herein, so that the desired result is obtained in the tissue. The practitioner applies one or more optical pulses to the treatment zone, moves the hand-piece to another area to be treated and repeats the application.

[0093] For example, the light source may be a diode or fiber laser operating at 1550 nm. As illustrated in **Fig. 20**, the laser 2002 is coupled into a fiber 2004 which terminates in a hand-piece 2006 that contains a lens 2008 or combination of lenses and a flat optical plate 2010 which is placed by the practitioner in close contact with the tissue surface 2016. The light emerges from the fiber, passes through the lens and then through the plate. The diode laser is set to deliver a pulse of light of precisely controlled power and pulse length. The lens collimates the light and the plate provides a small stand-off between the lens and the tissue, so that the lens is always the same distance from the tissue surface. In this way, a precisely controlled application of light creates a treatment zone 2018. Many variations of this basic design will be immediately apparent to one of ordinary skill in the art, and are embodiments of this invention. These include replacing the lens by a lens combination, as might be utilized to obtain high numerical apertures up to  $NA=1.0$  or even higher (if there is no air gap), and making the plate very thin. This high numerical aperture configuration may be used to create columnar zones in the manner described herein. Further, the plate may be omitted so that the lens or lens combination is in direct contact with the skin. Mirrors, holographic elements and

phase plates are some of the equivalent means of creating the degree and extent of focusing required to obtain the desired tissue treatment. The laser pulses are typically released into the fiber at time intervals controlled by the practitioner, through a button or equivalent on the hand-piece, or by a foot pedal (not illustrated). Alternately, a continuous wave (CW) laser beam is released into the fiber and a control mechanism is coupled to the output end of the fiber so that practitioner control is exercised at the fiber end just prior to the beam exiting the system. This embodiment "stamps" the laser pulses onto the tissue, one pulse and one zone at a time. The pattern of treatment zones is determined by the practitioner as he/she relocates the hand-piece between pulses. Alternately, the hand-piece may be in motion with intermittent firing of the laser either based on user control or by an automated system, with a constant repetition rate for firing the laser or a rate of repetition based on the movement of the hand-piece.

[0094] Another embodiment illustrated in **Figs. 21a** and **21b** utilizes the simultaneous stamping of many pulses through the use of a lens array. The light from the fiber 2104 passes through a close-packed array of lenses 2108 to create a number of treatment zones 2118 simultaneously. One advantage of the lens array is that it defines precisely the location of many treatment zones, and so fixes precisely the fraction of the tissue that is treated. Lens arrays may be fabricated as a simple array of normally refractive lenses cut or etched into a single transparent plate. Greater optical efficiency may be obtained using a diffractive optic such as a phase plate or zone plate in the manner of a Fresnel lens. Holographic approaches are also known. A lens array is just one of many means of realizing the embodiment of simultaneous stamping of many pulses. All such means are within the scope of the invention.

[0095] A further lens array embodiment includes the use of a silicon lens array to convert a single beam to an array of small treatment zones simultaneously within the skin such that rapid treatment can occur. As illustrated in **Fig. 21b**, these lenses can be placed in contact with the skin directly or through a contact window or plate to create a very high NA system if small treatment zones or high angles are desired, as in the case of deep dermal treatments. A second aspect of this embodiment is that a micro lens array can be built into an adapter tip that can be used to convert an existing medical laser device into a device with small treatment zones (<1mm diameter). Microlens arrays are commonly created using etching or molding materials such as glass or silicon. For example, companies such as MEMS Optical (Huntsville, AL) make etched silicon lens arrays and Corning (Corning, NY) and Lightpath Technologies, Inc. (Orlando, FL) molded glass lens arrays. Other materials such as UV cured epoxy

manufactured by Oriel Instruments division, Stratford, CT of Spectra Physics, Inc., Mountain View, CA, may be used. Diffractive elements such as those manufactured by Holographix, Inc. Hudson, MA, may also be used to form microlensing elements. In addition, an array of small GRIN lenses, such as may be manufactured by Dicon Fiber Optics, Inc., Richmond, CA, or other small lenses (Lightpath Technologies, Inc. Orlando, FL) could be joined together to create an array.

[0096] For certain applications of microscopic laser treatment, it is desirable to have a large area at the surface of the target area and a small area at the focal point of the laser system. This can be achieved by employing embodiments of the present invention that have a high numerical aperture lens system. If multiple spots are desired, and a conventional multiple separate adjacent lens system is used, there is a limit on how closely multiple lens elements may be packed together. Two filled individual lenses cannot be placed any closer than edge to edge without having their beams overlap. For a particular lens array with normal incidence relative to the target skin, this places a limit on how closely together their focal spots can be placed. As illustrated in Fig. 22, an embodiment of the present invention includes using a single large lens to create multiple spots within the skin in close proximity. This embodiment describes a design for creating multiple spots very close together using a single lens instead of a lens array. Multiple light beams (2204, 2206, 2208) are incident at different angles on a single large lens 2202 that focuses those beams to different places within the skin to create a treatment zone 2210. Multiple light beams can be incident on a spherical lens to create multiple spots within the skin. The beams come to different focal spots because they are incident on the lens at different angles. Other lens shapes and optical configurations will be evident to one skilled in the art, and these other lens shapes and optical configurations are alternate embodiments of the present invention.

[0097] A further embodiment of the invention uses a diode laser mounted together with the lens in the hand piece. The light from the diode lasers is directed to the tissue directly by a system of lenses and/or mirrors that may either reshape the beams or focus them, or both. Electrical and thermal conditioning of the diodes is typically more complex because the main power supply and a substantial part of the cooling mechanism may be placed remotely. Alternately, the power supply and cooling mechanism may be placed within the handpiece.

[0098] A further embodiment is a variation on the lens array design, and includes directing the laser beam from a single laser sequentially from one lens to the next, or one irradiation site to the next, by a scanning device. Thus, the power of the laser is directed for a short time to each



lens or to each site, in contrast to the case of simultaneous illumination of all the lenses, where the laser power is divided between the lenses and sites. For a fixed laser power and treatment energy per site, the total time the laser is emitting optical energy is the same in the sequential and simultaneous cases. However, the time of irradiation of any one site is much shorter for sequential illumination than for simultaneous illumination. A short pulse length is often advantageous for controlling the shape of the treatment zones. While many effects in tissue depend on the total energy delivered, or the peak temperature reached, there are other effects that depend on the rate of heating. For example, the electrical response of nociceptor cells lies in this latter category. Thus, the pulse length may significantly influence the experience of pain by the patient. We have already described the role that pulse length may have in expanding the diameter of columnar zones. If the pulse length is limited by this (or another) consideration then sequential illumination is a means of reducing the power of the optical source and thereby reducing the cost and the size (footprint) of the irradiation hardware.

[0099] As illustrated in **Fig. 23**, a further embodiment is to locate the laser remotely, and sequentially scan the beam(s) using a scanner 2308 and a single lens 2314. The scanner may reside between the lens and the tissue 2310, or it may reside between the lens and the output of the optical fiber 2304. The scanner 2308 directs the optical energy to different sites in a predetermined sequence. The scanner may utilize any suitable method of redirecting a laser beam, such as acousto-optic deflectors, MEMS devices, galvo-activated mirrors, or rotating mirrors. In one embodiment, a pair of galvo-driven mirrors redirects the laser beam after it emerges from the fiber, and before it passes through a lens that creates a sharp focus below the surface of the skin. The parameters of the scanner, such as its location, angular variation or beam-center motion, may be determined by well-known optics formulae and are well-understood by those skilled in the art. Scanners have the advantage over static systems in that they may be designed to correct for blurring of the treatment zone along the direction of motion of the hand-piece as the hand-piece moves over the skin surface. The parameters describing the motion of the hand-piece may be obtained using a sensor and optical mouse technology. In particular a scanner may be configured to correct real-time for the specific motion caused as the practitioner moves the hand-piece over the tissue surface. The scanner 2308 may be one-dimensional or two-dimensional. The scanner may also be in the third-dimension along an axis parallel to the optical axis so as to create a scanning of the depth of focus of the system.

[0100] Further embodiments may also be envisaged by one of ordinary skill according to the conventions of the field, and the teachings presented here. For example, the use of several lasers, pulsing together or in sequence, allows parallelism in the treatment of many sites. It also allows some variation in the wavelength used in the treatment protocols. For example, using several different wavelengths enables the treatment zone to be elongated. As illustrated in **Fig. 24**, if several lasers are used, the sites they are directed to can be arranged to lie along a line perpendicular to the direction of motion of the hand-piece over the tissue. The sites in this 'collinear set' are illuminated substantially simultaneously. If the 'collinear set' concept is combined with a scanner that moves the entire set of sites, as a group, in the direction of motion of the hand-piece over the skin, such a scanner can be designed to correct for blurring as well. This combination of a collinear set fixed in relation to each other, but scanned as a group in a direction perpendicular to the mathematical line joining them has several attractive features, including reducing the mechanical accelerations in the scanner while de-blurring the laser spots. The collinear set may also be illuminated non-sequentially, randomly or in an interleaved manner to allow for heat dissipation between adjacent treatment sites between treatments of those adjacent sites.

[0101] A further alternate embodiment of the present invention includes counter-rotating elements or wheels with optical elements on the counter-rotating elements such that one or more beams passing through the optical elements are deflected and/or focused in a desired direction. Examples of such systems are described in co-pending U.S. Patent Application Serial Nos. 10/750,790, filed on December 31, 2003, and 10/751,041, filed on December 23, 2003, both of which are incorporated herein by reference.

### **Experimental results and Histology**

[0102] The following table (Table 2) shows examples of average results for various system parameters for embodiments of the present invention.

Table 2

| Wavelength<br>(nm) | Pulse Energy<br>(mJ per pulse) | Focus in air<br>(from contact<br>window)<br><br>(mm) | Average<br>Treatment Depth<br>(microns) | Average<br>Treatment<br>Diameter<br>(microns) |
|--------------------|--------------------------------|--|---|---|
|                    |                                |  |   |   |

|      |      |     |     |     |
|------|------|-----|-----|-----|
| 1535 | 10   | 0.3 | 375 | 90  |
| 1550 | 11   | 0.3 | 610 | 85  |
| 1535 | 12   | 0.3 | 380 | 98  |
| 1550 | 13.5 | 0.3 | 600 | 95  |
| 1535 | 20   | 0.3 | 575 | 125 |
| 1550 | 22.5 | 0.3 | 700 | 125 |

[0103] The depths and diameters are for the necrotic zones and are averages. This data is offered by way of example only and the present invention is not limited to these values. The speed of treatment may be as much as 10 cm per second, and preferably in a range between about 2 cm/second and 6 cm/second. The stratum corneum may be spared using this embodiment and these parameters, or it can be damaged and/or removed, especially if the contact window is removed and/or the wavelength is changed. Additionally, treatment depths achieved may be as much as 100-200 microns deeper than shown as averages in the Table 2 above. Alternate embodiments listed above may produce similar results for depth, width and aspect ratio. However, each embodiment will have differing treatment speeds, pattern densities, precision, ease of use and efficacy.

[0104] Typical system parameters across embodiments include: wavelengths in a range between about 500 nm and about 4,000 nm, and preferably between about 1,000 nm and about 3,000 nm, and more preferably between about 1400 nm and about 1600 nm; pulse energies in a range up to about 150 mJ per pulse, and preferably up to about 50 mJ per pulse; an optical treatment beam cross-sectional width at the tissue surface in a range less than about 500 microns, and preferably in a range less than about 200 microns; a numerical aperture for the system in a range between about 0.005 and about 2.0, and preferably in a range between about 0.01 and about 1.0; a focal depth measured from the tissue surface in a range between about 500 microns above the tissue surface and about 2 mm below the tissue surface, and preferably in a range between about 200 microns below the tissue surface and about 1500 microns below the surface; a pulse duration in a range between about 50 microseconds and about 100 milliseconds, and preferably in a range between about 400 microseconds and about 10 milliseconds; for embodiments that include scanning means, a speed of movement of the hand-

piece or the optical beams across the surface of the tissue in a range less than about 10 cm per second, and preferably in a range between about 2 cm per second and about 6 cm per second; and a speed of treatment zone (i.e. necrotic zone and/or HSZ) formation of at least about 100 treatment zones per second, preferably in a range between about 500 treatment zones per second and about 2000 treatment zones per second, and more preferably in a range between about 1000 treatment zones per second and about 1500 treatment zones per second. In scanner systems, the speed of movement of the hand-piece may not be correlated directly with hand movement, especially in embodiments with intelligent robotics using mouse control. The typical results for embodiments employing these parameters typically include the following:

depth of treatment up to about 4 mm below the surface; a treatment zone diameter of less than about 1 mm, and preferably less than about 500 microns; an aspect ratio of at least 1:2, and preferably an aspect ratio of at least about 1:4; a treatment zone density in a range up to about 2500 treatment zones per square centimeter per pass of the device across the tissue, and preferably in a range up to about 1000 treatment zones per pass of the device across the tissue; and a separation between the centers of adjacent treatment zones of at least 50 microns, and preferably at least about 150 microns.

[0105] As illustrated in **Figs. 25a** and **25b**, embodiments of the present invention have been used on human tissue to produce substantially columnar treatment zones that span the epidermal-dermal junction 2510 and spare the stratum corneum 2502. Different system parameters would not spare the stratum corneum, and such sparing of the stratum corneum is not required for all embodiments or treatments. The following parameters were used in treating the tissue shown in Figs. 25a and 25b: wavelength of 1500 nm and a pulse energy of 5 mJ. Fig. 25a shows the results within one hour after treatment. The stratum corneum 2502 remains intact, the epidermis 2504 is fully coagulated and necrosed, and a substantially columnar thermal wound 2508 is seen in the dermis 2512. A separation in the dermal-epidermal junction 2510 is sometimes seen here as well. The width of the treatment zone is largely uniform throughout the depth of the treatment zone and measures about 80-100 microns. The depth of the wound is about 200-300 microns. Fig. 25b shows the results of the treatment and the healing response 24 hours post-treatment. In Fig. 25b, the epidermis 2504 is largely re-epithelialized in the treated area 2514, dermal repair is continuing in and around the thermal wound area 2516, and often a microscopic epidermal necrotic debris (or MEND) (not shown) has formed under the stratum corneum. The MEND consists typically of necrotic debris from treatment and epidermal pigment. The MEND typically flakes off in less than a week.

[0106] The foregoing describes a system and method for laser surgery wherein a focused optical signal such as a laser, LED, or an incoherent source of optical energy is advantageously created to achieve microscopic treatment zones. Further, the foregoing describes a method and apparatus wherein a focused optical signal can be used to treat sub-epidermal regions without  
5 damaging epidermal regions. Persons of ordinary skill in the art may modify the particular embodiments described herein without undue experimentation or without departing from the spirit or scope of the present invention. All such departures or deviations should be construed to be within the scope of the following claims.

What is claimed is:

1. A method for achieving beneficial effects in a target tissue in skin comprising treating the target tissue using optical radiation to create a plurality of microscopic treatment zones in a predetermined treatment pattern, wherein a subset of said plurality of discrete microscopic treatment zones includes individual discrete microscopic treatment zones comprising necrotic tissue volumes having an aspect ratio of at least about 1:2.
2. The method of claim 1, wherein the microscopic treatment zones are separated by thermally unaltered tissue.
3. The method of claim 1, wherein the microscopic treatment zones are surrounded by thermally altered heat shock zones comprising viable tissue.
4. The method of claim 3, wherein the heat shock zones are separated by thermally unaltered tissue.
5. The method of claim 1, wherein the microscopic treatment zones extend from the skin surface up to 4 mm into the tissue.
6. The method of claim 1, wherein the microscopic treatment zones extend from the skin surface to the epidermal-dermal junction.
7. The method of claim 7, wherein the microscopic treatment zones have a depth measured from the epidermal-dermal junction of the skin in a range up to about 4 mm into the dermis.
8. The method of claim 1, wherein the necrotic tissue volumes have a cross-sectional width in a range between about 10  $\mu\text{m}$  and about 1,000  $\mu\text{m}$ .
9. The method of claim 8, wherein the necrotic tissue volumes have a cross-sectional width in a range between about 25  $\mu\text{m}$  and about 750  $\mu\text{m}$ .
10. The method of claim 9, wherein the necrotic tissue volumes have a cross-sectional width in a range between about 50  $\mu\text{m}$  and about 500  $\mu\text{m}$ .
11. The method of claim 2, wherein the cross-sectional width of the viable heat shock zone is controlled by the predetermined treatment pattern.

12. The method of claim 1, where the predetermined treatment pattern of creating the microscopic treatment zones is accomplished by choosing one or more variables from the list comprising laser wavelength, chromophore, laser energy density, pulse energy, pulse duration, thermal diffusion constants and the temporal and spatial distribution of the laser energy.
- 5 13. The method of claim 12, wherein the chromophore is water.
14. The method of claim 12, wherein the pulse energy is less than about 150 mJ and the pulse duration is in a range between about 50 microseconds and about 100 milliseconds.
15. The method of claim 12, wherein the pulse energy is less than about 50 mJ and the pulse duration is in a range between about 400 microseconds and about 10 milliseconds.
- 10 16. The method of claim 1, wherein the ratio of the sum of the volumes of the microscopic treatment zones to the target tissue volume is less than one.
17. The method of claim 1, wherein the microscopic treatment zones have a physically intact stratum corneum.
18. The method of claim 1, wherein the necrotic tissue volumes are substantially columnar.
- 15 19. The method of claim 1, wherein the aspect ratio is greater than about 1:4.
20. A method for achieving beneficial effects in skin tissue comprising treating the tissue by exposing a targeted part of the tissue to optical radiation to create a plurality of microscopic treatment zones such that the volume of the target tissue that remains substantially unaffected by the optical radiation is controlled.
- 20 21. The method of claim 20 wherein the control is achieved by focusing the optical radiation to desired depths in the skin.
22. The method of claim 20 wherein each microscopic treatment zone is thermally altered by the optical exposure.
23. The method of claim 20 wherein each microscopic treatment zone is surrounded by a heat shock zone comprising viable tissue.
- 25

24. The method of claim 20 wherein the microscopic treatment zone includes a necrotic tissue volume defined by a cross-sectional width in a range between about 10  $\mu\text{m}$  and about 1,000  $\mu\text{m}$  and a depth of up to about 4 mm in the direction of the optical radiation.
25. The method of claim 20 comprising choosing a target region, using a hand piece to deliver  
5 laser energy to the target region, where the target region is treated by the movement of the hand piece over the target region when the area of the target region is greater than the cross sectional area of the hand piece.
26. The method of claim 20, wherein a subset of said plurality of discrete microscopic treatment zones includes individual discrete microscopic treatment zones comprising necrotic  
10 tissue volumes having an aspect ratio of at least about 1:2.
27. A system for providing dermatological treatment comprising:  
a source of optical radiation;  
a means for delivering the optical radiation to a target volume of skin;  
a control system that is operably connected to the source of optical radiation and the  
15 means for delivering the optical radiation;  
the control system programmed to control the delivery of optical radiation to the target volume to create one or more microscopic treatment zones such that the volume of the target tissue that remains substantially unaffected by the optical radiation is controlled.
28. A system for providing dermatological treatment, comprising:  
20 a source of optical radiation;  
a delivery system operably coupled to the source, the delivery system configured to direct said optical radiation to a volume of tissue in a predetermined pattern; and  
wherein the predetermined pattern comprises a plurality of discrete microscopic treatment zones, wherein a subset of said plurality of discrete microscopic treatment zones  
25 includes individual discrete microscopic treatment zones comprising necrotic tissue volumes having an aspect ratio of at least about 1:2.
29. The system of claim 28, further comprising a source control system operably coupled to the source, the source control system configured to control a parameter of the optical radiation, wherein the parameter of the optical radiation includes at least one of wavelength, pulse  
30 duration, pulse energy, pulse shape, beam profile, chirp and repetition rate.
30. The system of claim 28, wherein the optical radiation has a beam cross-sectional width at the tissue surface of less than about 200 microns.



31. The system of claim 28, further comprising a delivery system controller operably coupled to the delivery system, the delivery system controller configured to control at least one of a plurality of delivery system parameters, the plurality of delivery system parameters including numerical aperture, focal length and optical radiation beam direction.
- 5 32. The system of claim 31, wherein the plurality of delivery system parameters further comprise scan speed, scan direction, de-blurring, number of optical radiation beams emitted simultaneously and pattern shape.
33. The system of claim 28, further comprising a contact window located between the delivery system and the tissue, and configured to contact the tissue when the system is in operation.
- 10 34. The system of claim 33, wherein the contact window comprises a material that is substantially transparent to the optical radiation and that has a high thermal conductivity.
35. The system of claim 33, wherein the source of optical radiation, the delivery system and the contact window are configured to cause a necrotic volume in an epidermal region within the tissue while substantially sparing a stratum corneum region adjacent to the epidermal  
15 region.
36. The system of claim 28, wherein the delivery system further comprises an optical system which includes at least one of a mirror, a lens, a lens array, a diffractive element, a holographic element and a fiber optic element.
37. The system of claim 36, wherein the optical system has a numerical aperture greater than  
20 about 0.005 and a focal point located in a range between about 500 microns above the tissue surface and about 1500 microns below the tissue surface.
38. The system of claim 28, wherein the delivery system further comprises a scanner system which includes at least one of a one-dimensional scanner and a two-dimensional scanner.
39. The system of claim 38, wherein the scanner system includes at least one of an acousto-  
25 optic element, a piezoelectric element, a galvanometer, a micro-electro-mechanical system (MEMS), a rotating mirror, a rotating prism, an optical mouse and a mechanical mouse.
40. The system of claim 28, wherein the necrotic tissue volumes have a diameter at the tissue surface of less than about 200 microns.

41. The system of claim 28, wherein the necrotic tissue volumes have a depth of at least about 200 microns.
42. The system of claim 28, wherein the discrete microscopic treatment zones have a physically intact stratum corneum.
- 5 43. The system of claim 28, wherein the discrete microscopic treatment zones are substantially columnar.
44. The system of claim 28, wherein the centers of the necrotic zones for the discrete microscopic treatment zones are separated by at least 50 microns.
45. The system of claim 28, wherein the predetermined pattern includes uniformly spacing the  
10 discrete microscopic treatment zones.
46. The system of claim 28, wherein the predetermined pattern includes a total number of discrete microscopic treatment zones in a range up to about 2500 per square centimeter.
47. The system of claim 28, wherein the optical radiation has a wavelength in a range between about 400 nm and about 12,000 nm, an energy up to about 150 mJ per pulse and a  
15 pulse duration up to about 100 milliseconds.
48. The system of claim 28, wherein the optical radiation has a wavelength in a range between about 900 nm and about 3,000 nm, an energy up to about 50 mJ per pulse and a pulse duration in a range between about 400 microseconds and about 10 milliseconds.
49. The system of claim 28, wherein the individual discrete microscopic treatment zones  
20 include heat shock zones, the heat shock zones and the necrotic tissue volume for the individual discrete microscopic treatment zones form a substantially cylindrical combined volume, the substantially cylindrical combined volume has an aspect ratio of at least about 1:1.
50. The system of claim 28, wherein the ratio of the sum of the surface areas of necrotic tissue and heat shock zone to the sum of the surface area of untreated tissue within the target tissue  
25 volume is less than one.
51. The system of claim 28, wherein the source of optical radiation comprises one or more of a fiber laser, a diode laser, a carbon-dioxide laser, a diode-pumped solid state laser, a ruby laser, and optical parametric oscillator or an excimer laser.

52. The system of claim 28, wherein the system causes an optical fluence incident on the surface of the tissue in a range between about 0.001 Joules per square centimeter and about 100,000 Joules per square centimeter.

53. The system of claim 28, wherein the aspect ratio is greater than about 1:4.

- 5 54. The system of claim 28, wherein the delivery system further comprises a handpiece, the system configured to produce up to 2500 necrotic tissue volumes per square centimeter while the handpiece is moving at a speed in a range between about 1 centimeter per second and about 6 centimeters per second.

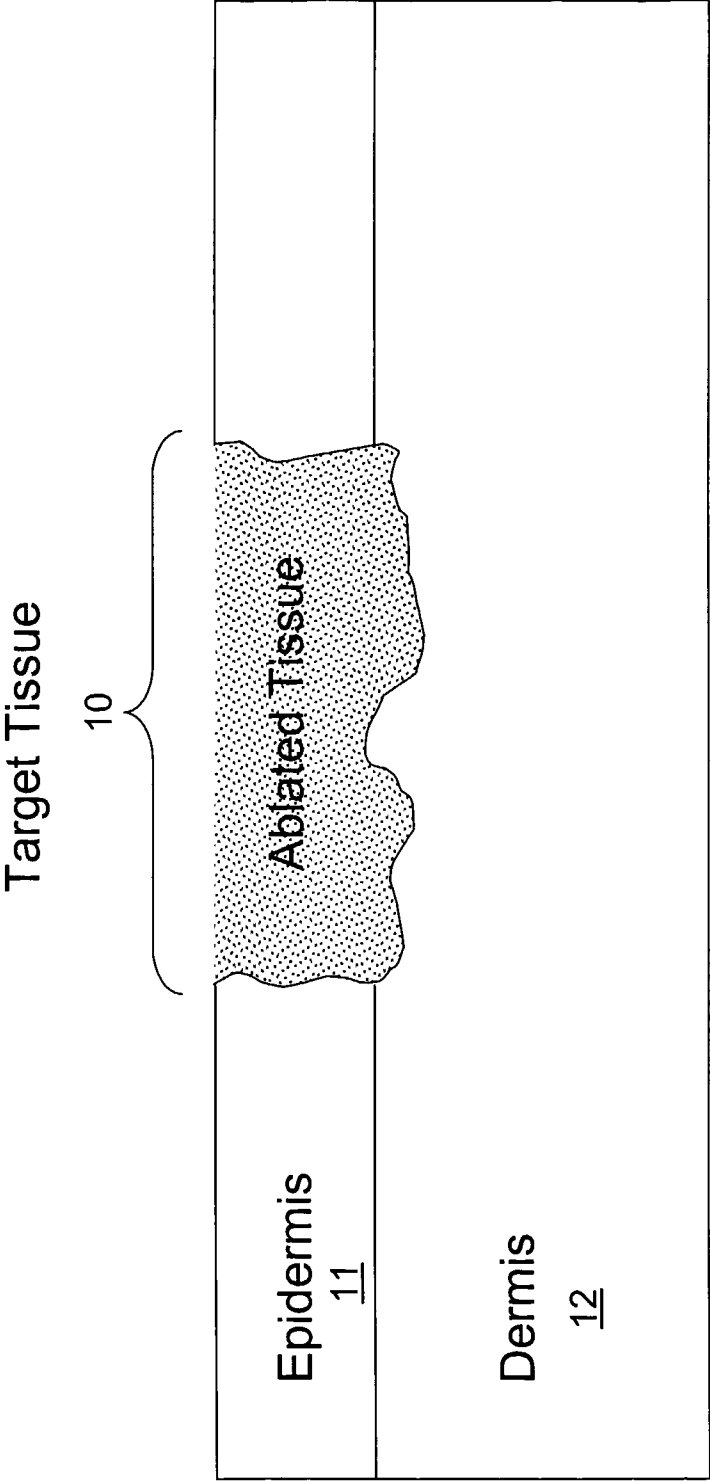
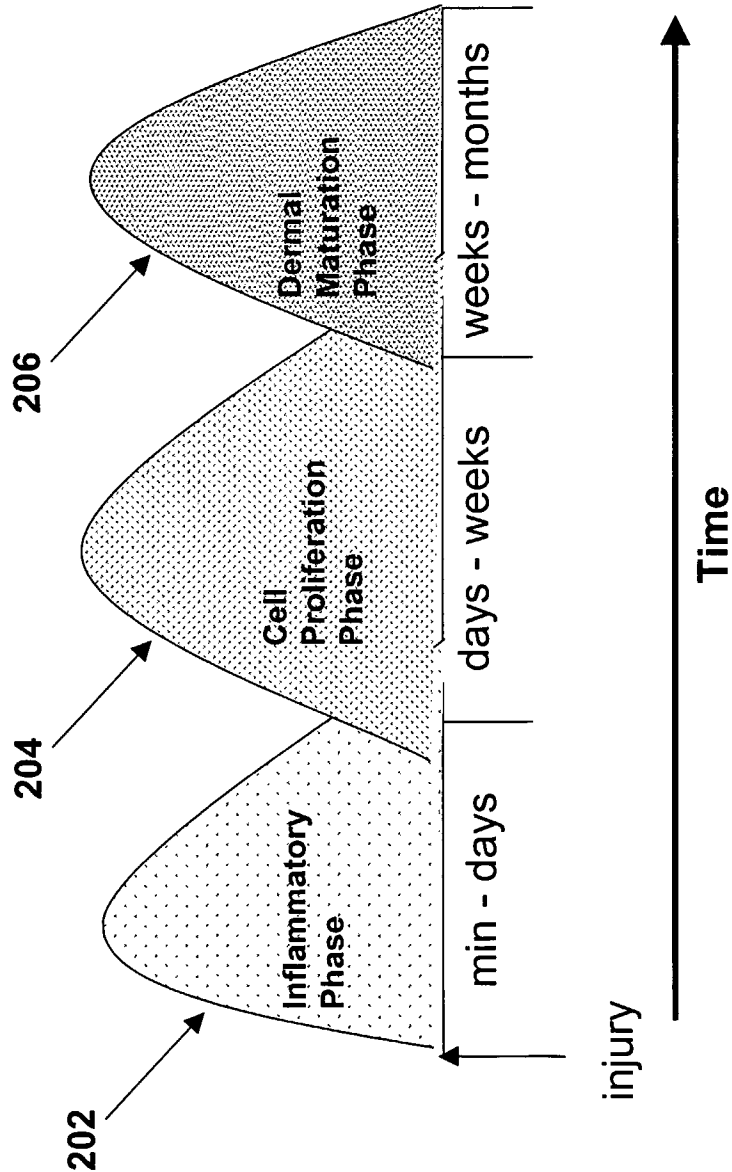
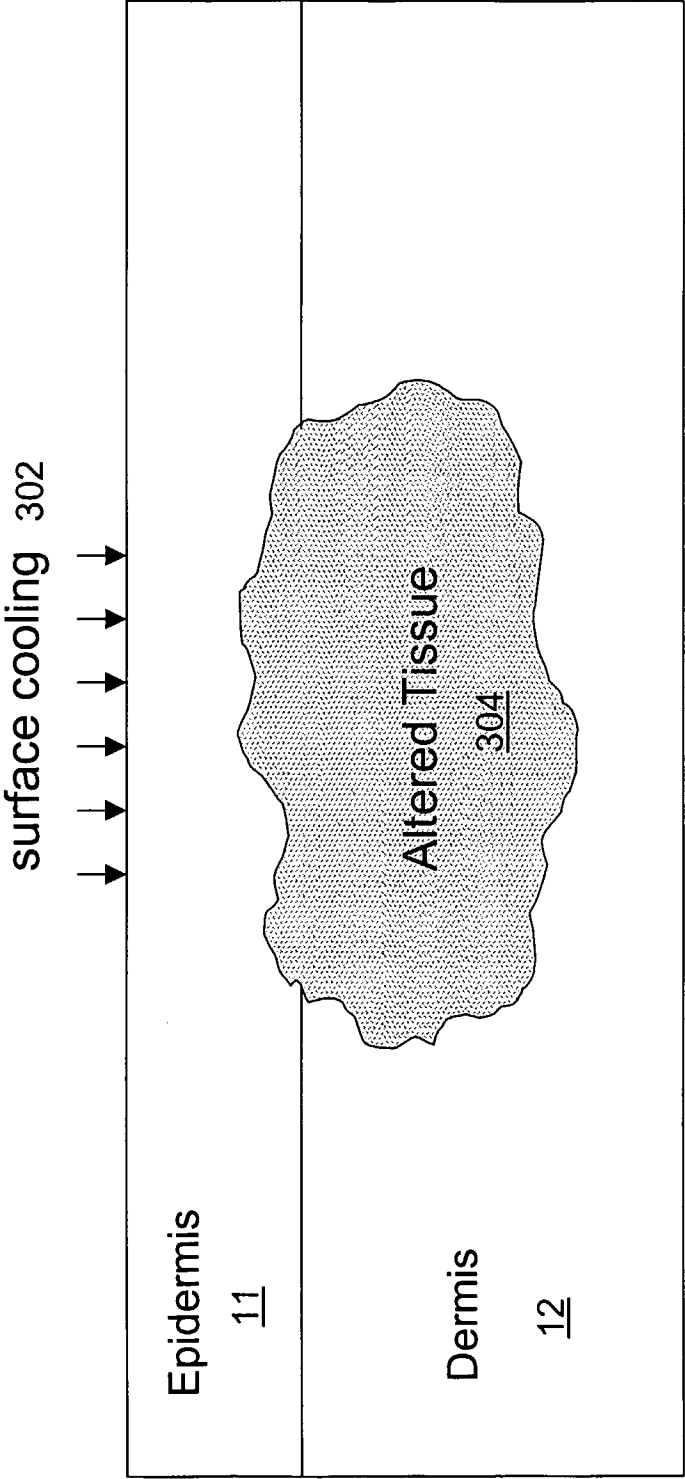


FIG. 1  
Prior Art



**FIG. 2**  
**Prior Art**



**FIG. 3**  
**Prior Art**

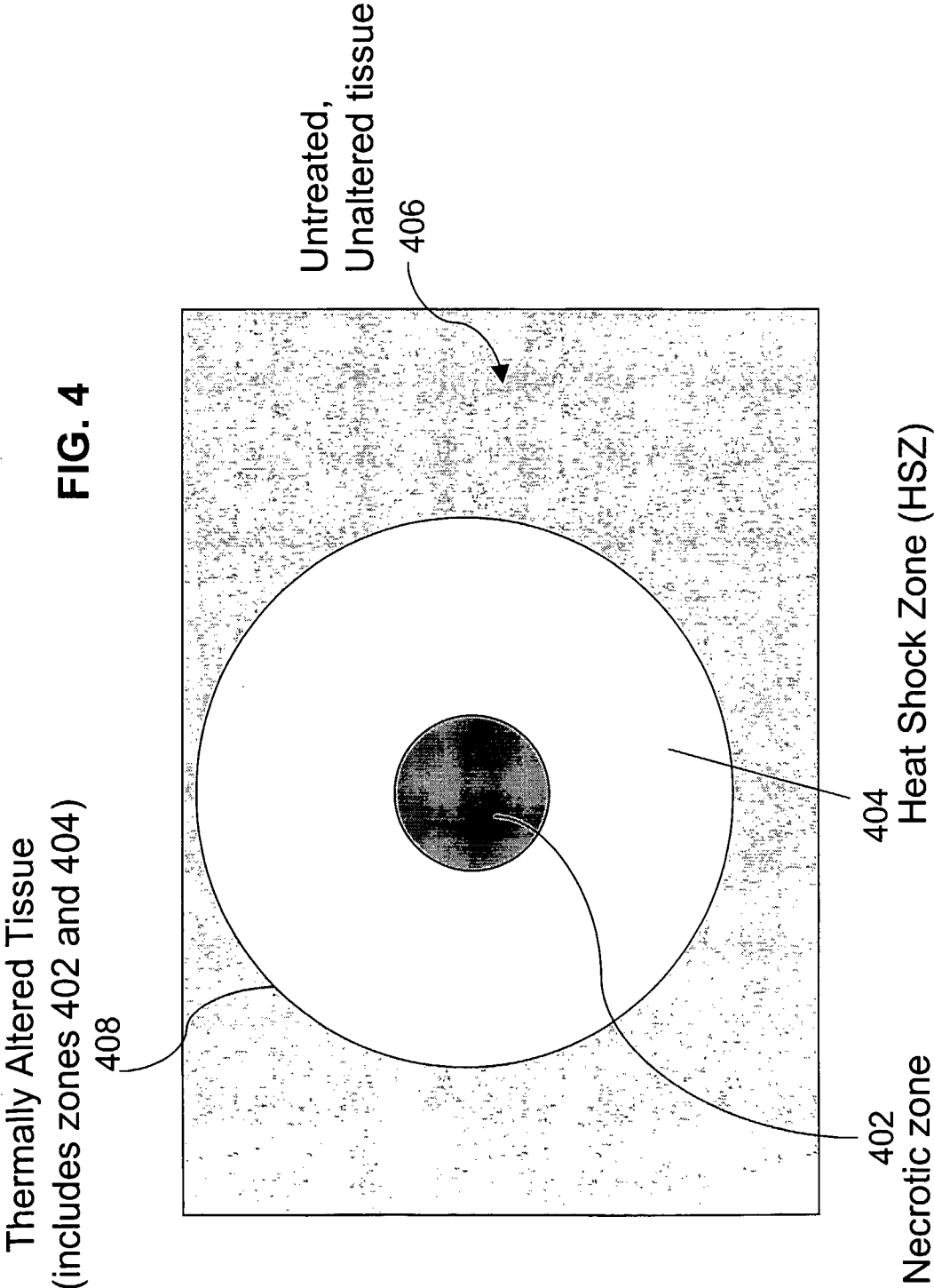
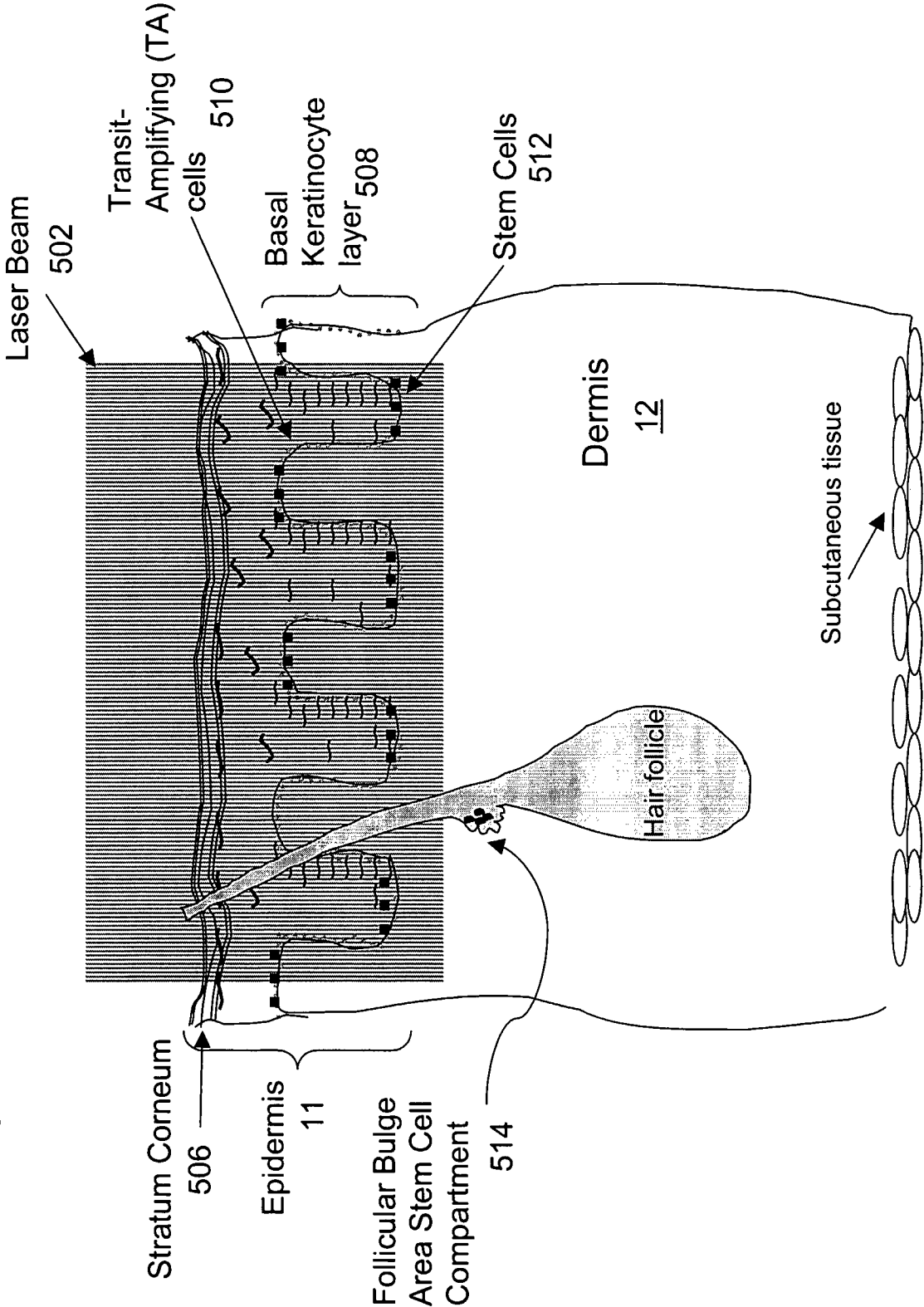


FIG. 5

Prior Art





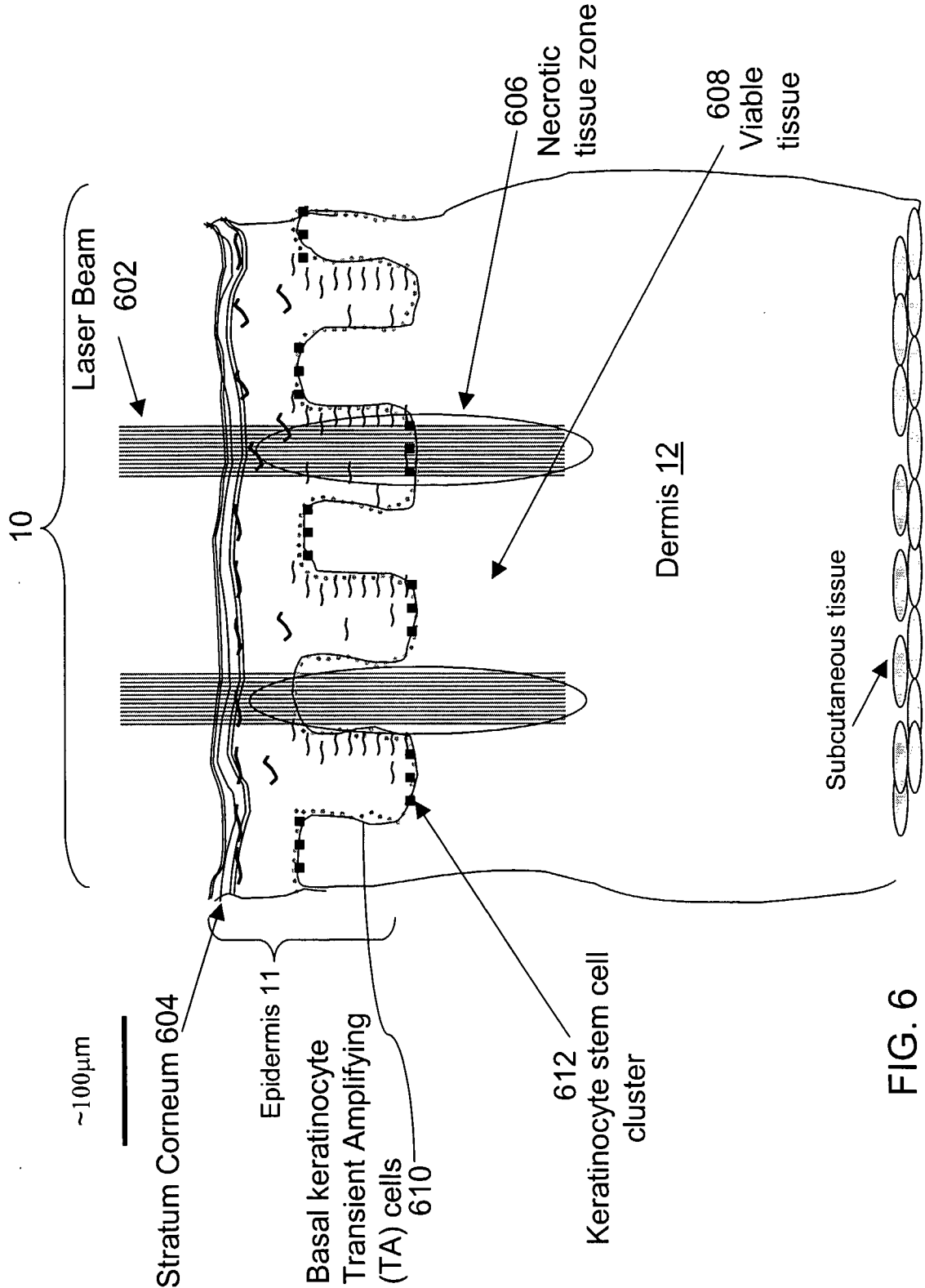


FIG. 6

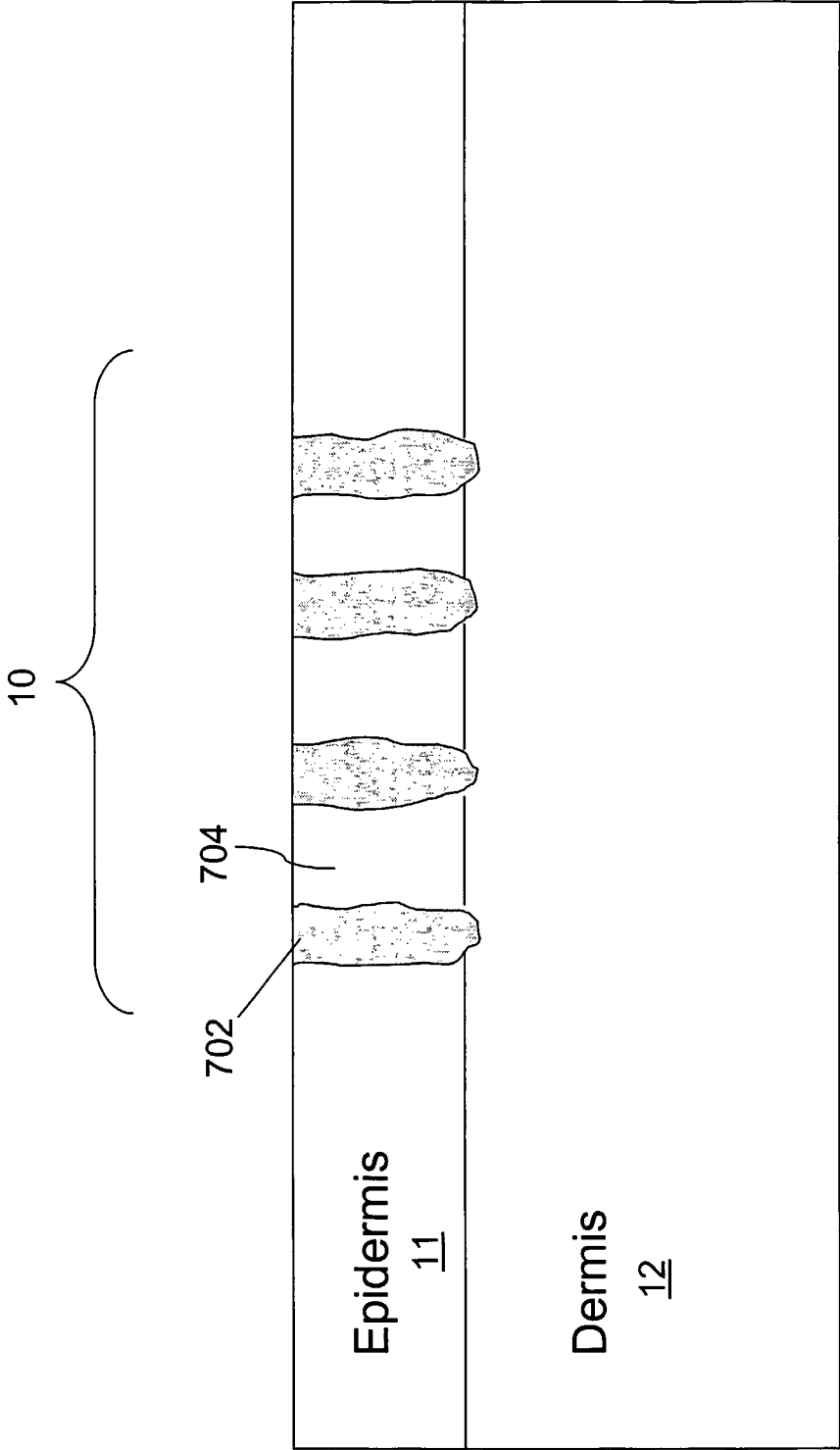


FIG. 7

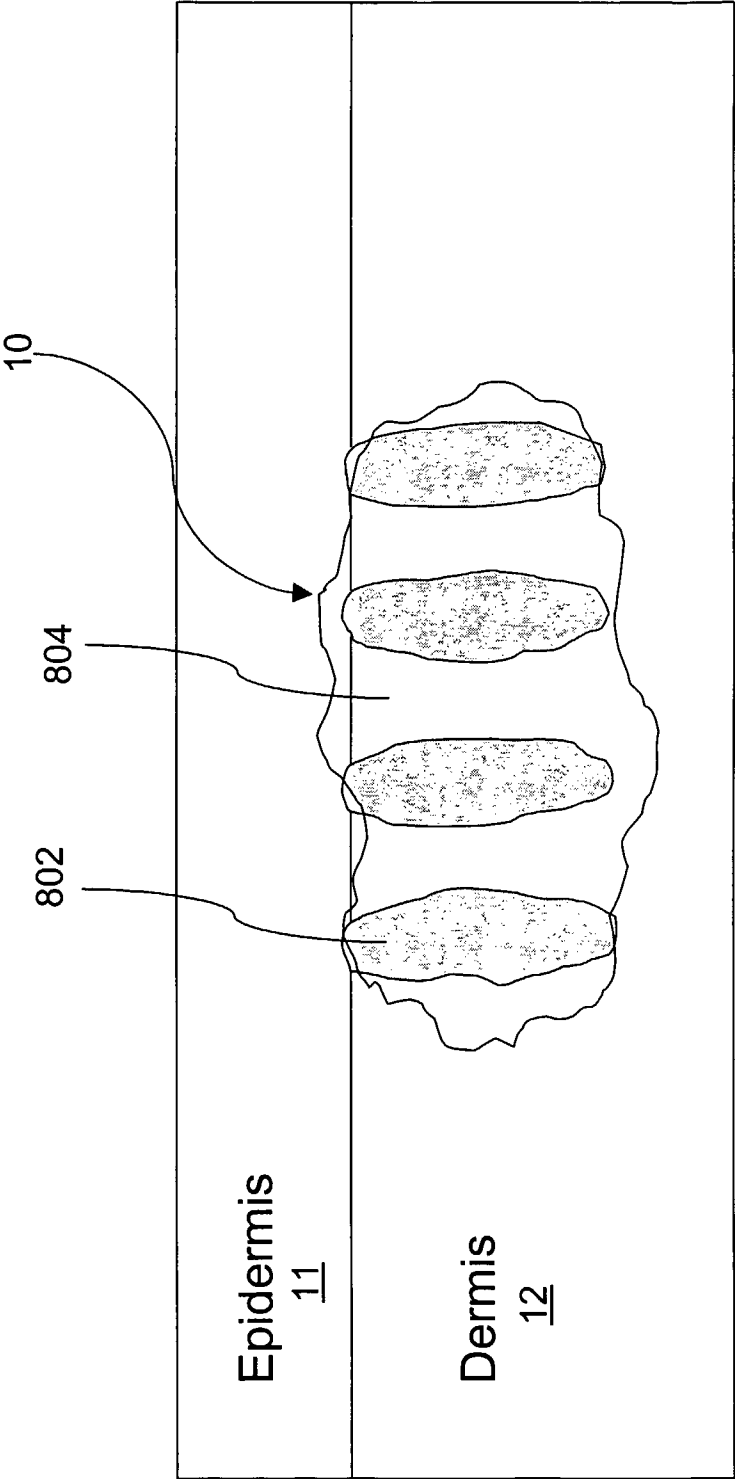


FIG. 8

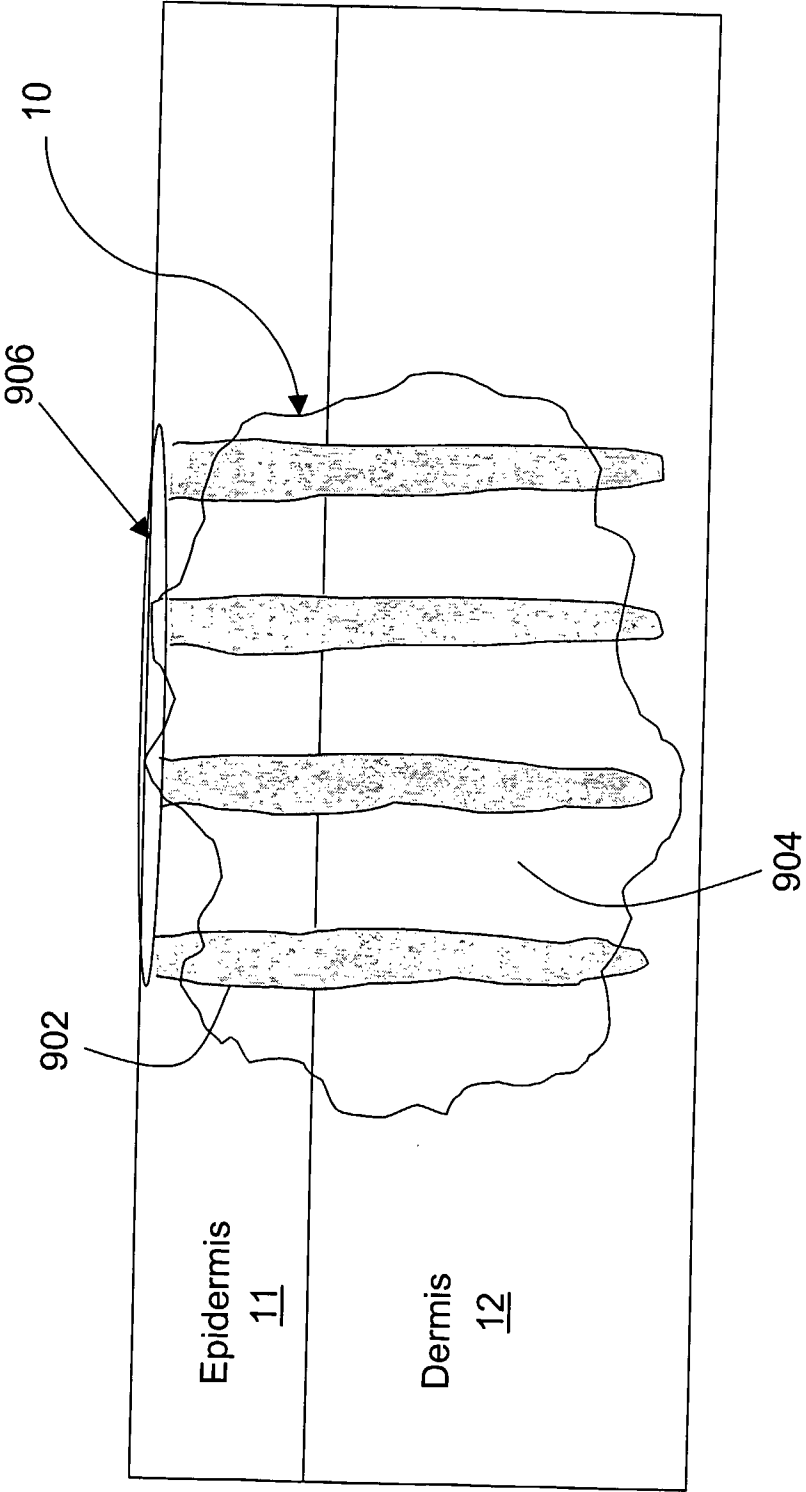
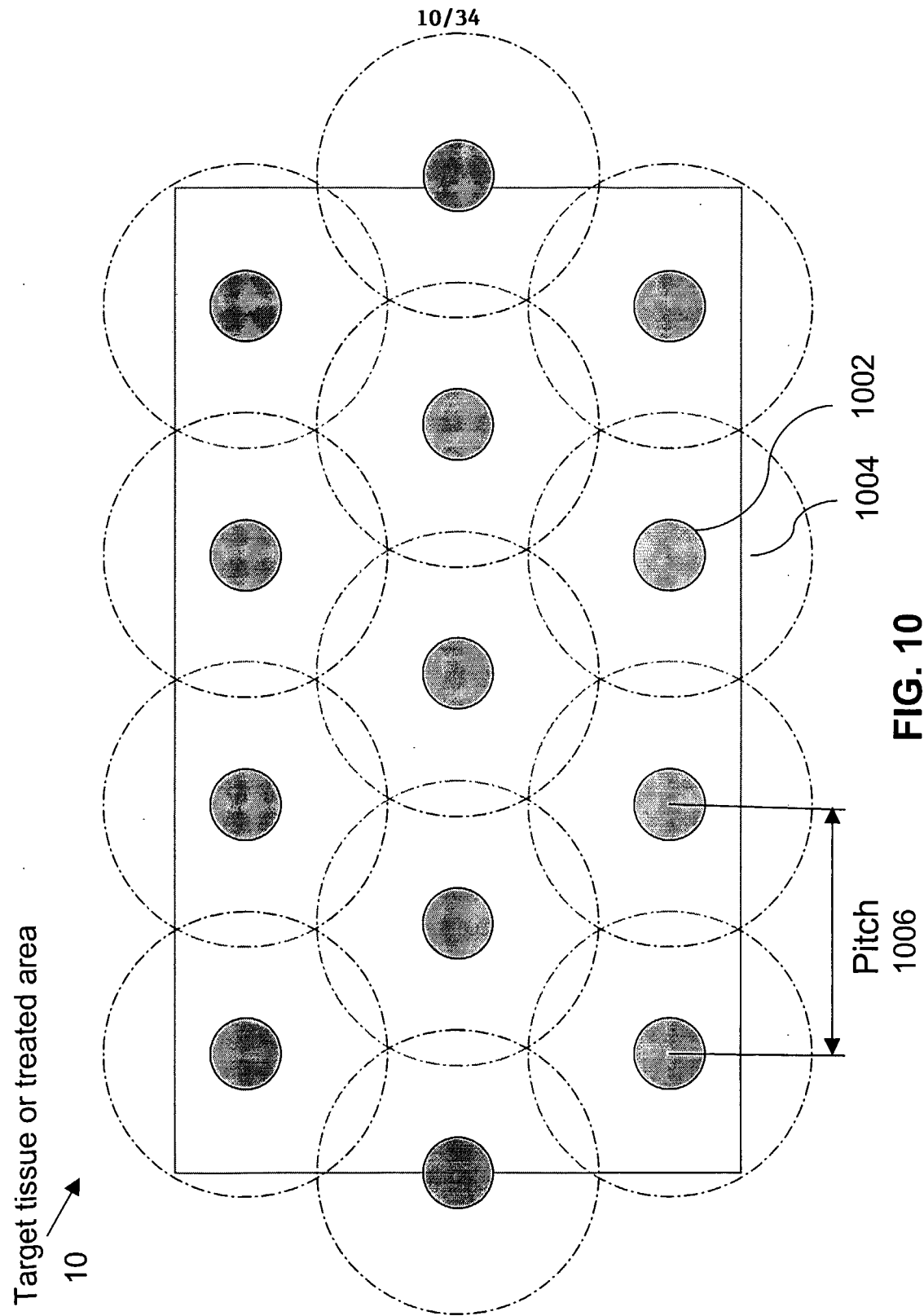


FIG. 9



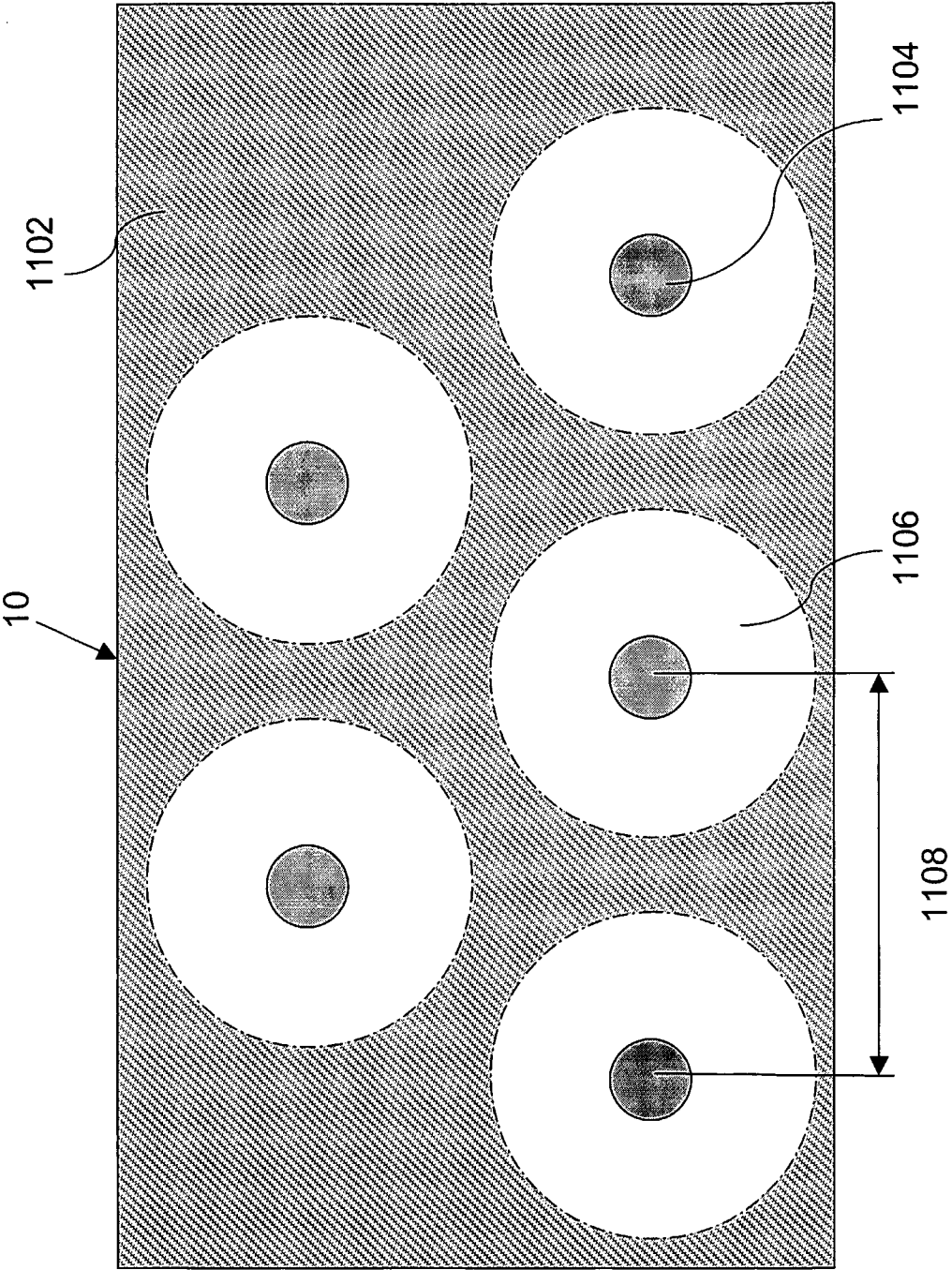


FIG. 11

Fig. 12a

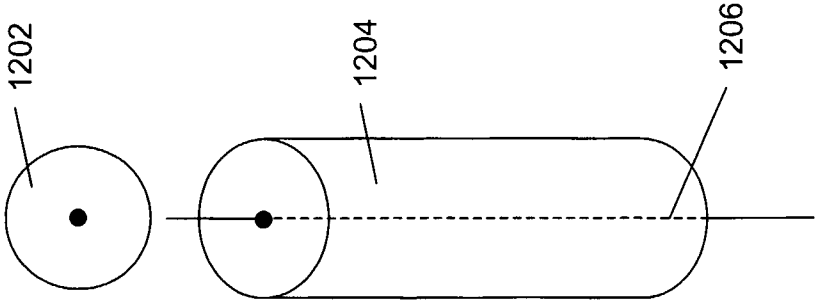


Fig. 12b

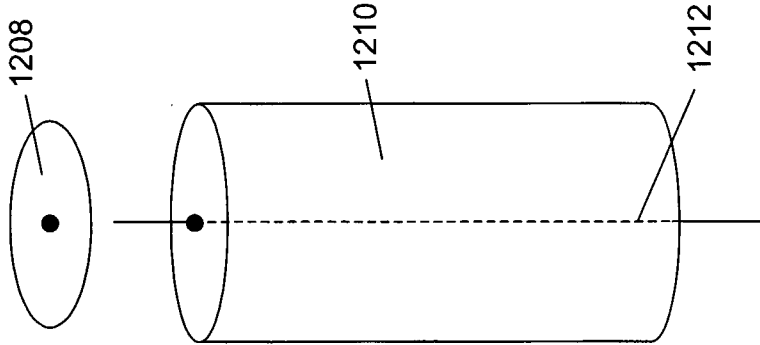


Fig. 12c

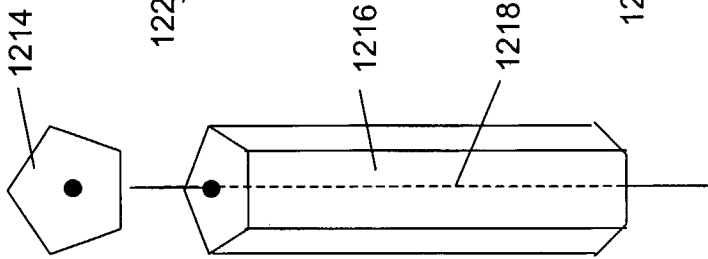


Fig. 12e

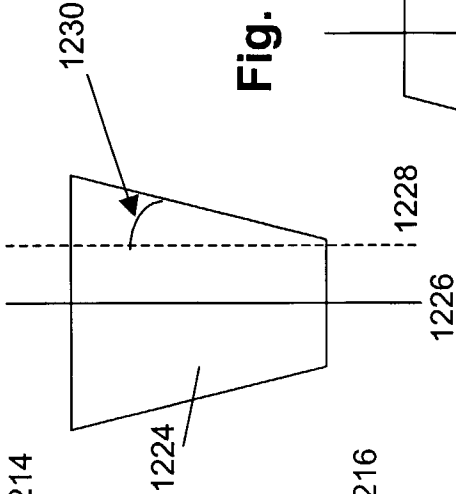


Fig. 12f

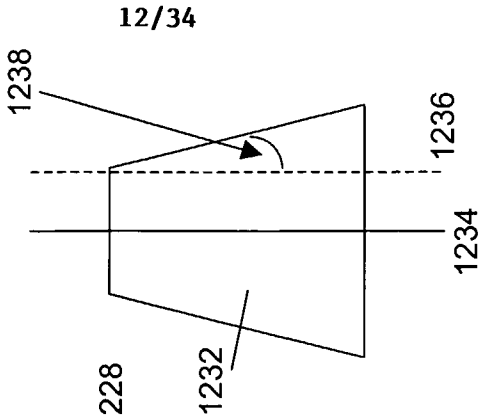


Fig. 12d

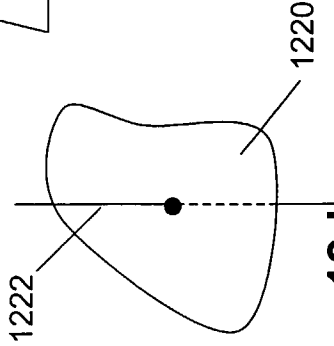


Fig. 12h

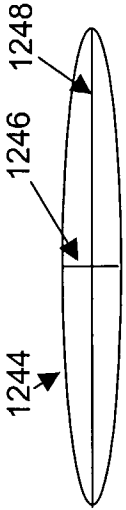
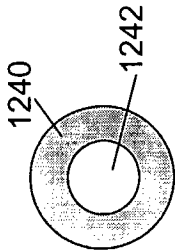
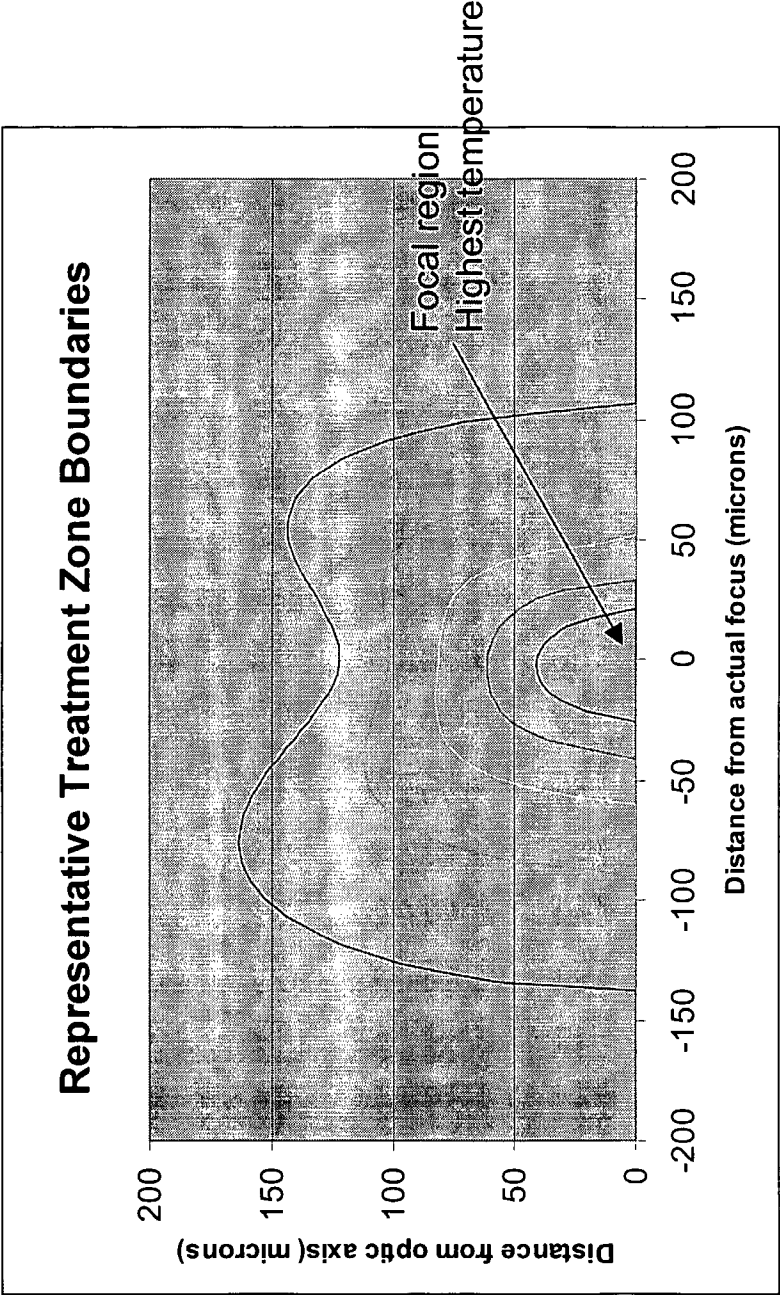


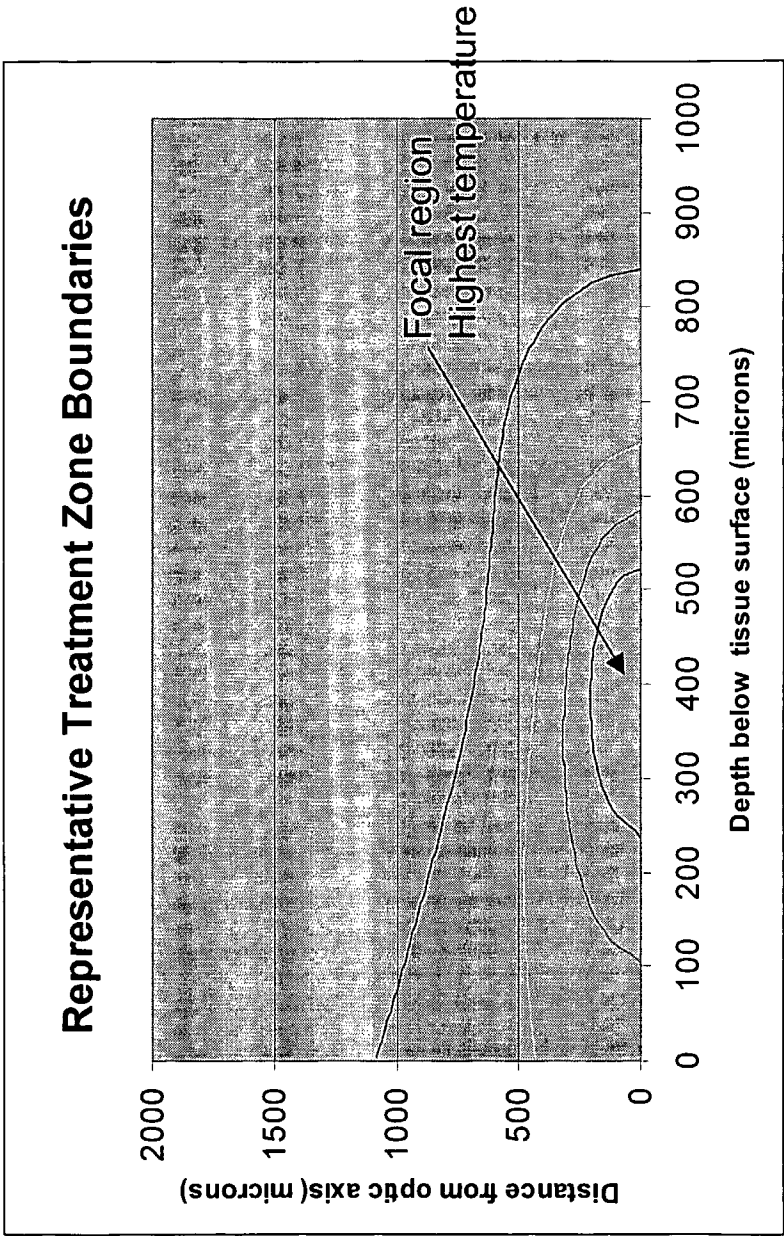
Fig. 12g



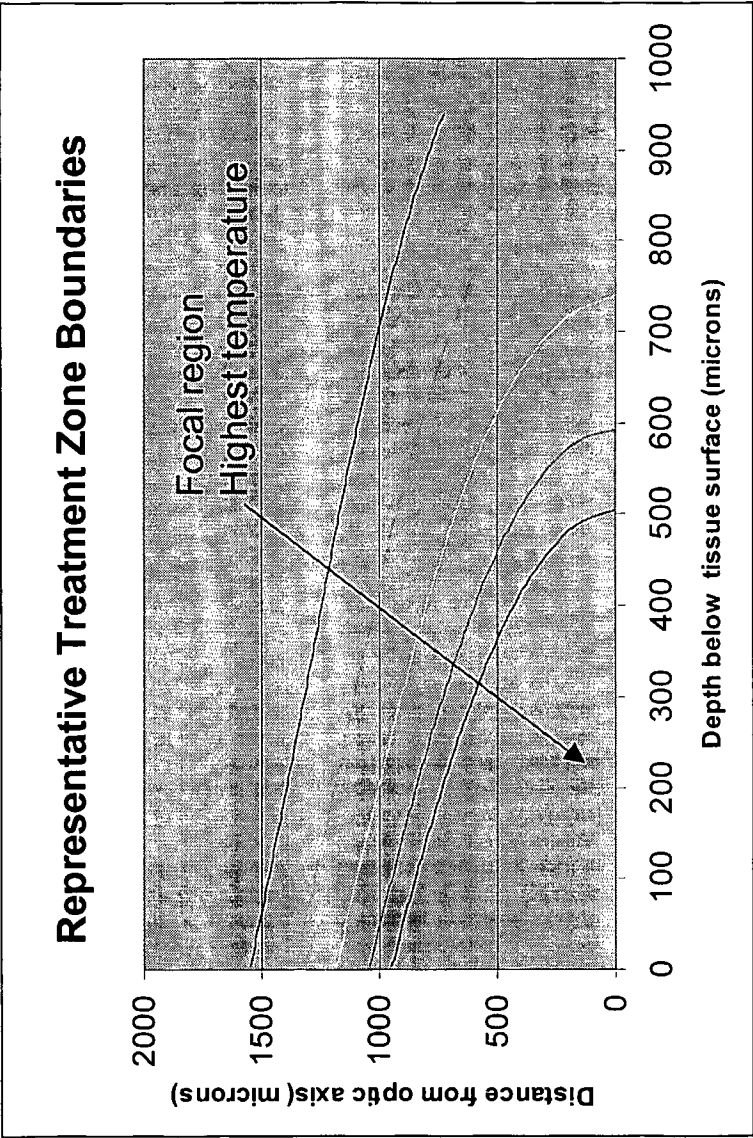


**Fig. 13a**





**Fig. 13b**



**Fig. 13c**

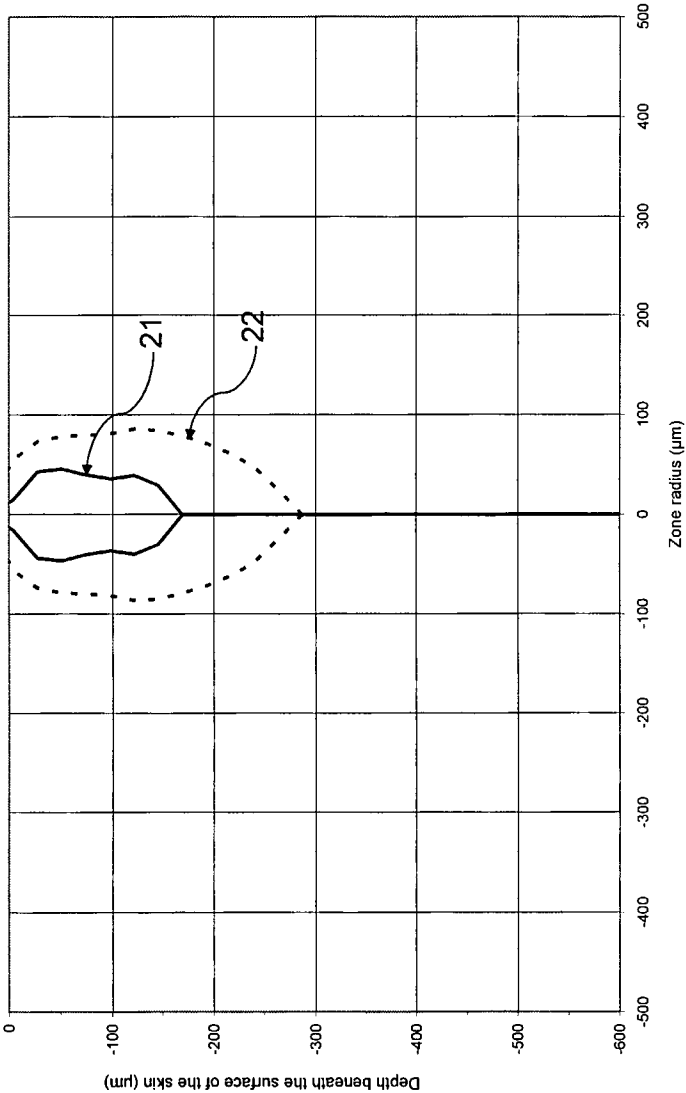


Fig. 14a

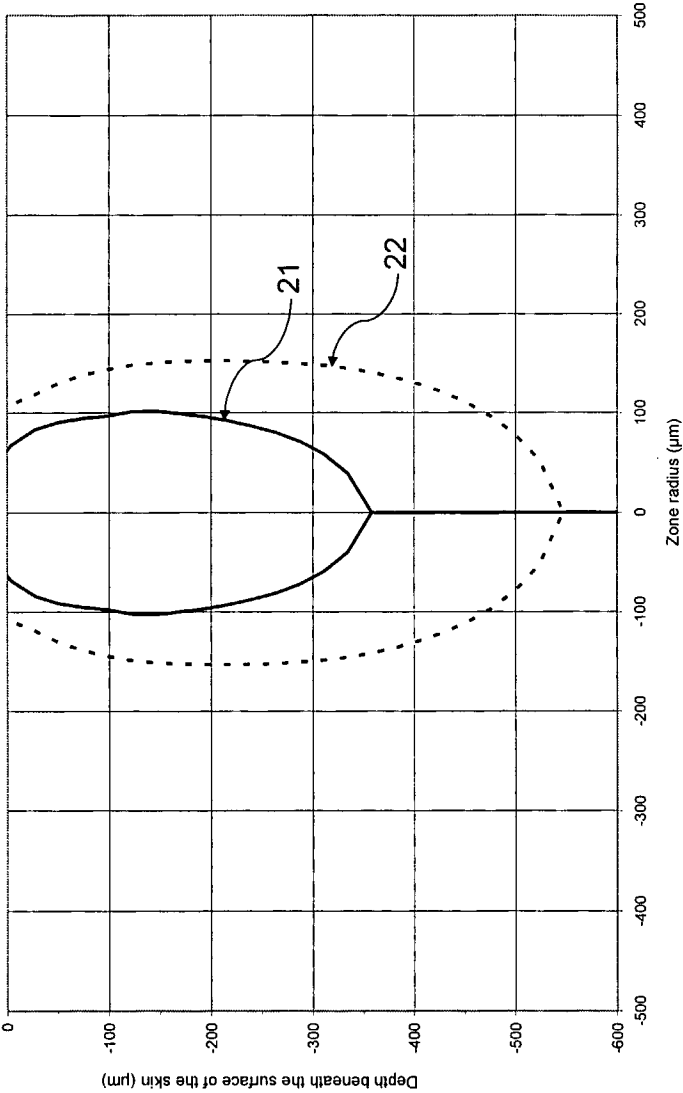


Fig. 14b

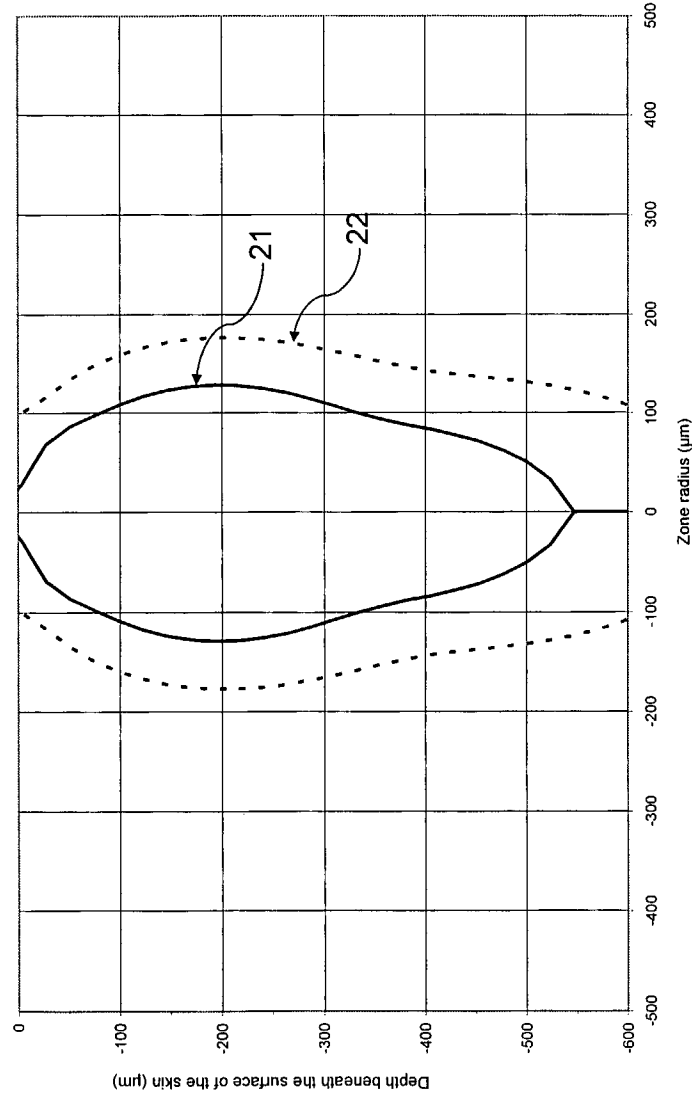


Fig. 14c

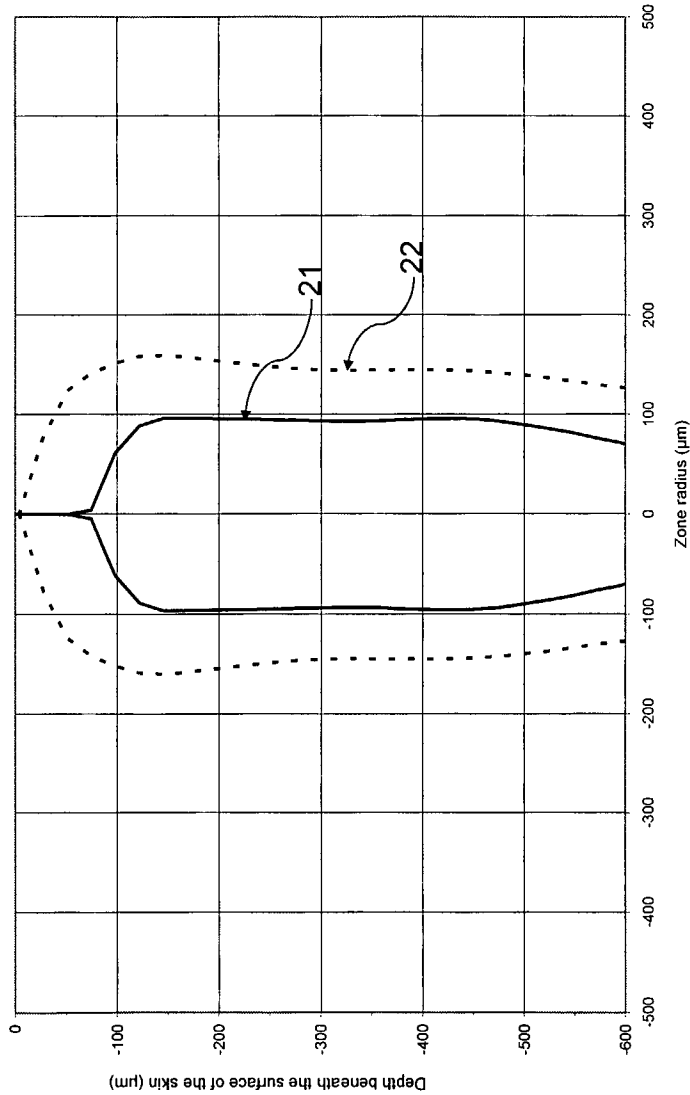


Fig. 14d

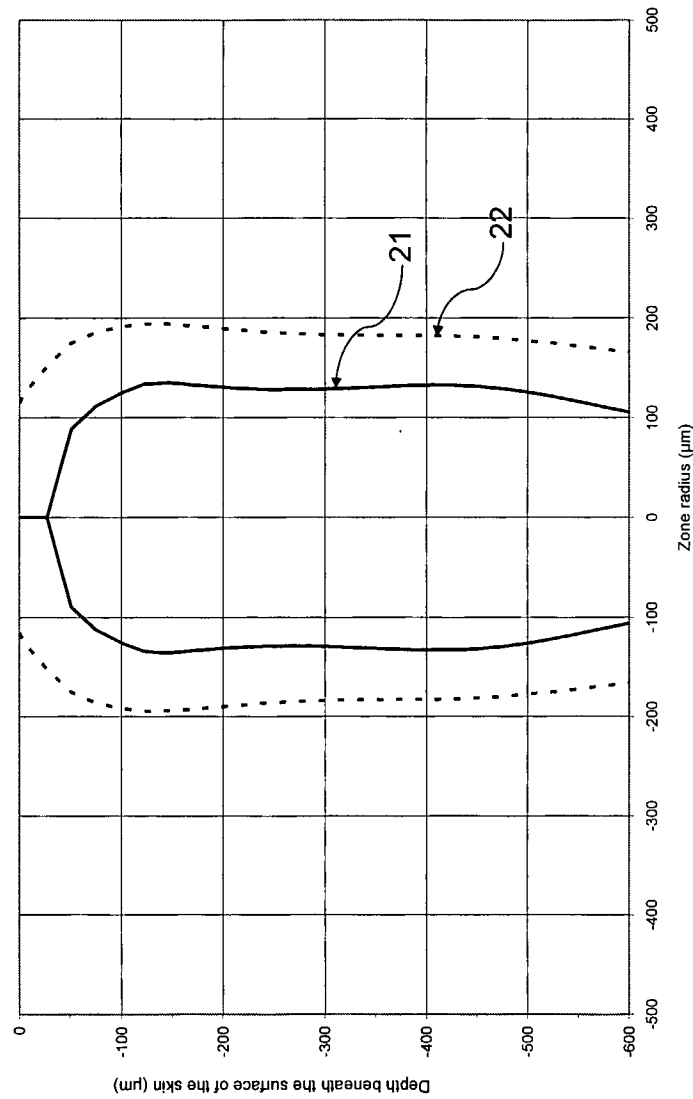


Fig. 14e

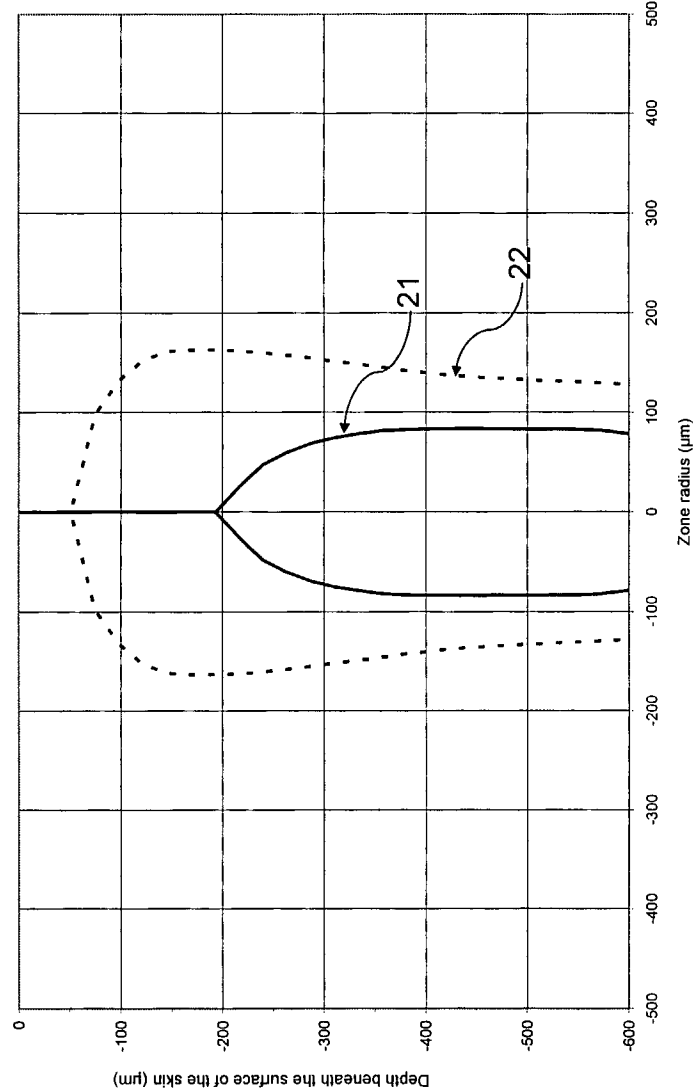


Fig. 14f



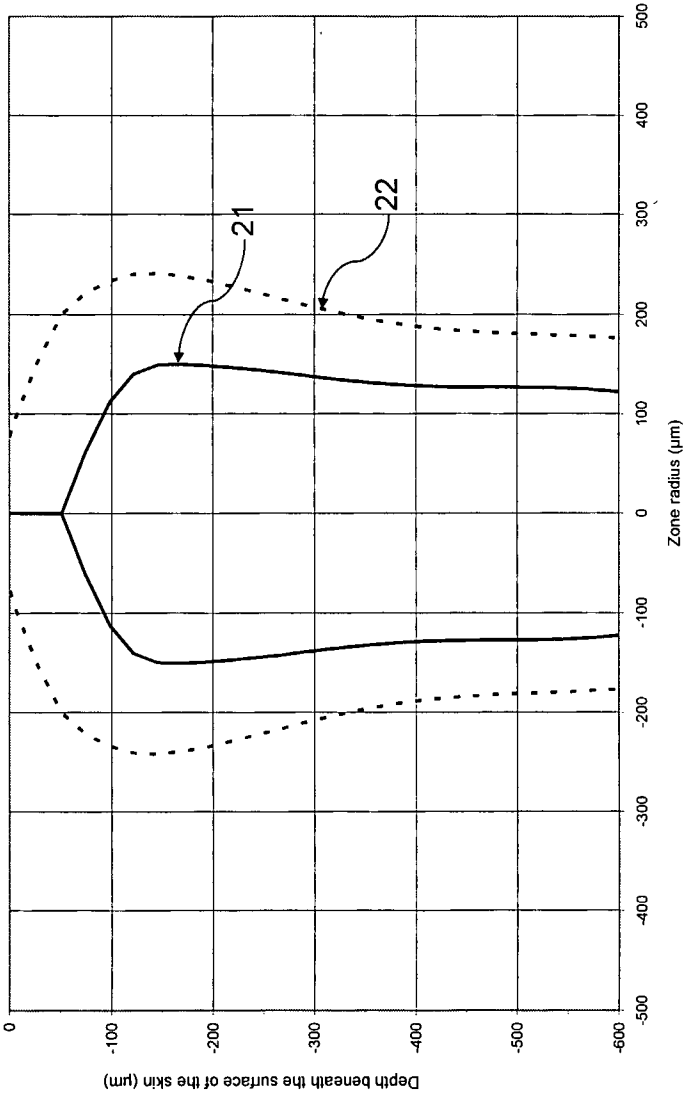


Fig. 14g

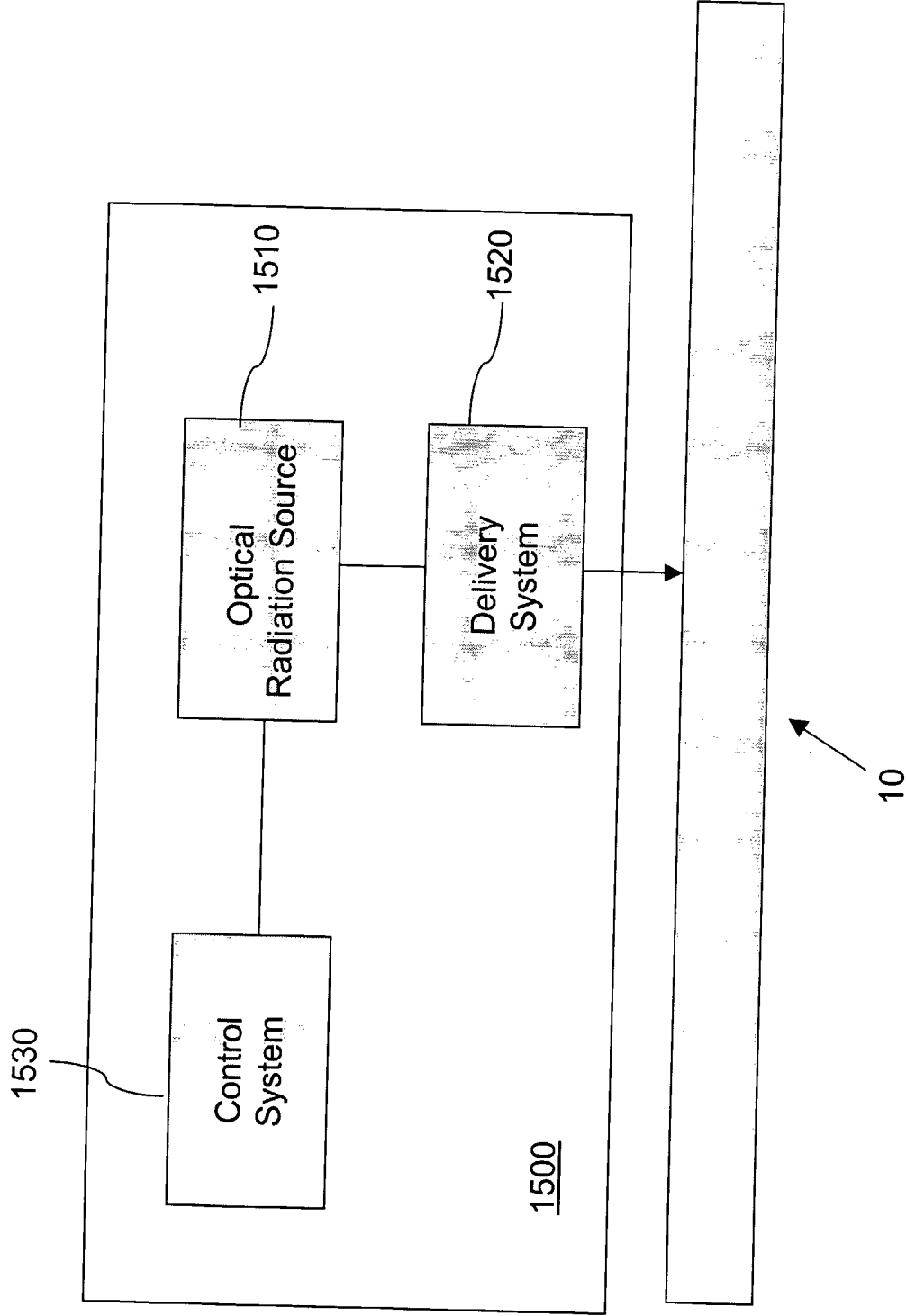


FIG. 15

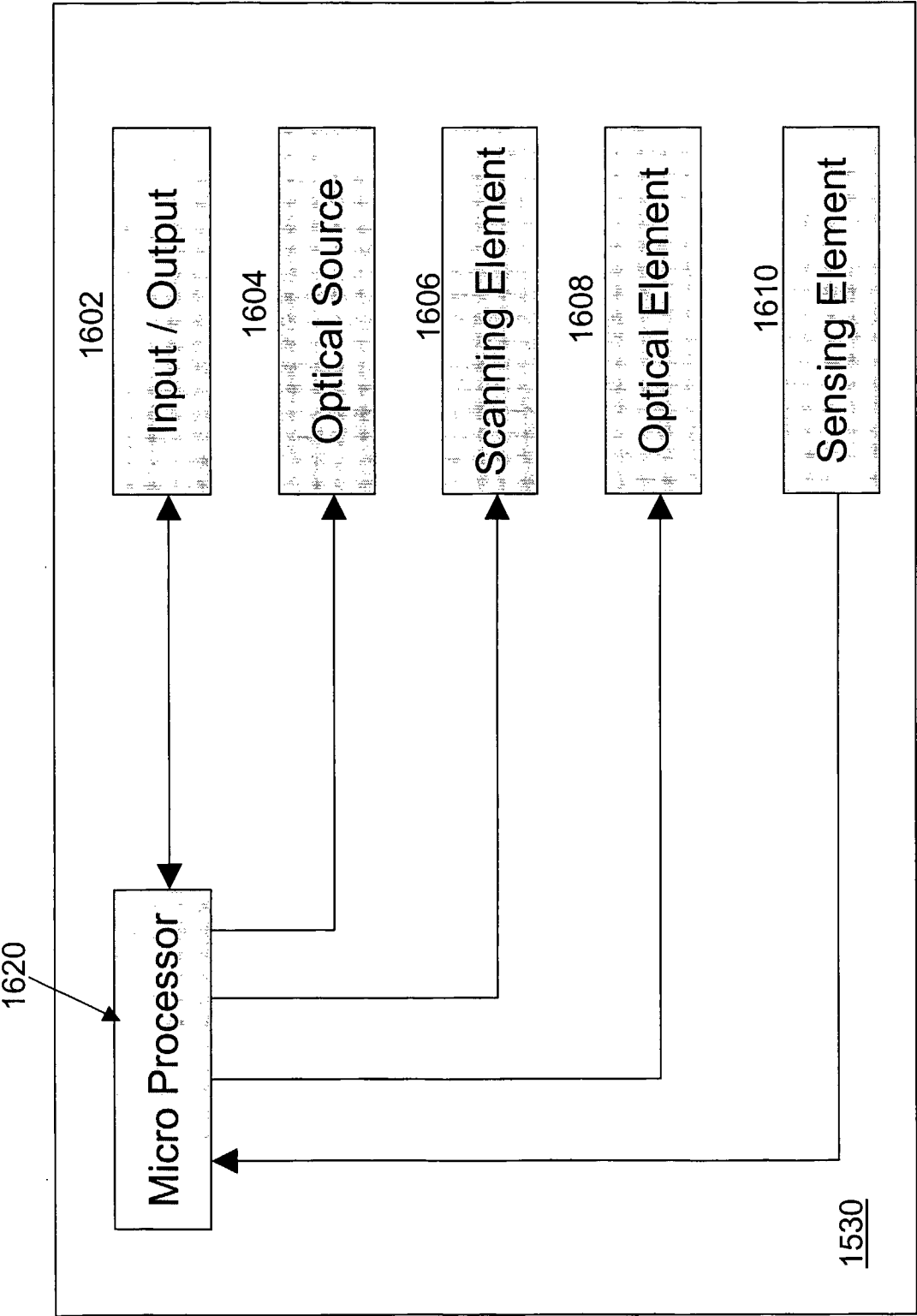
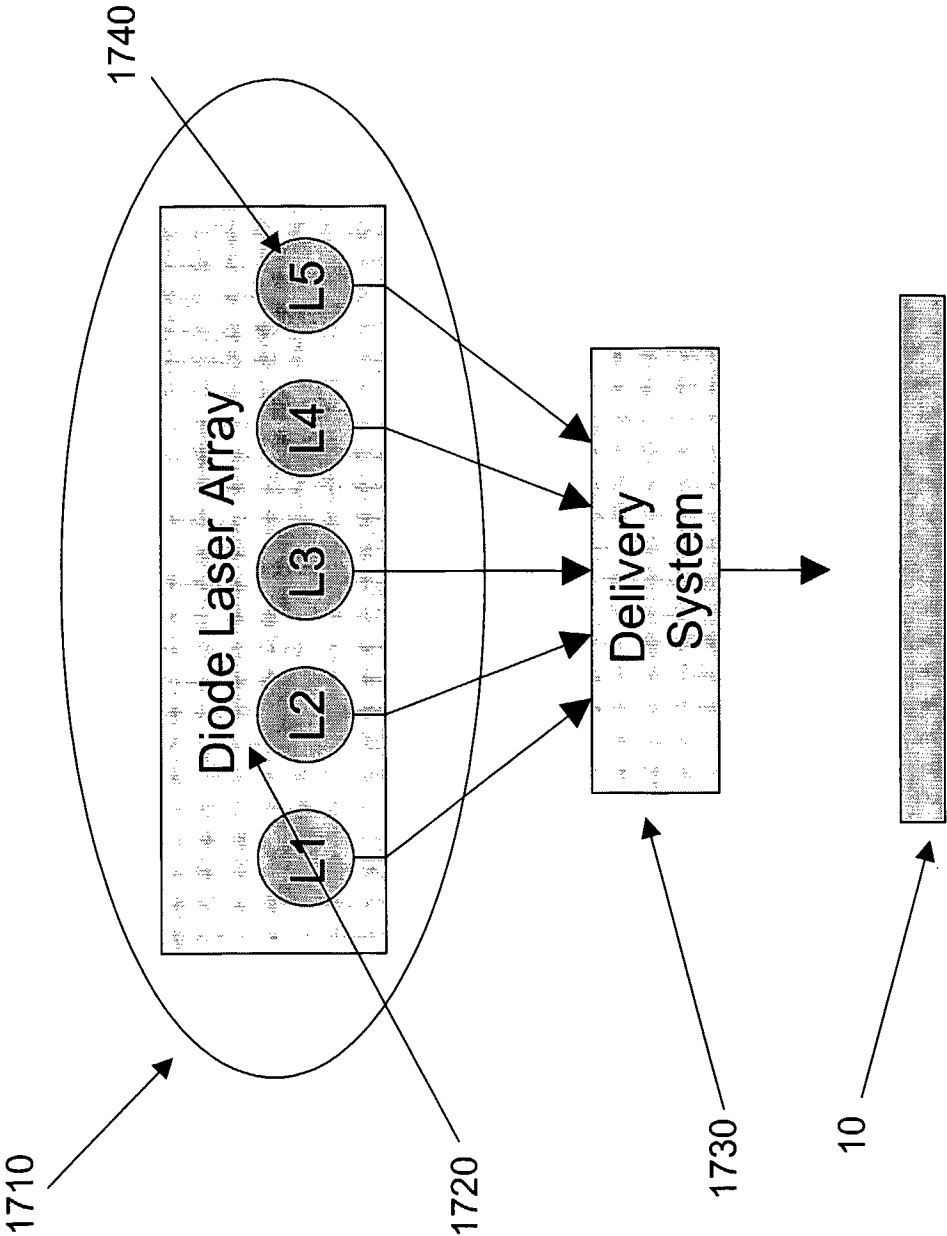


FIG. 16



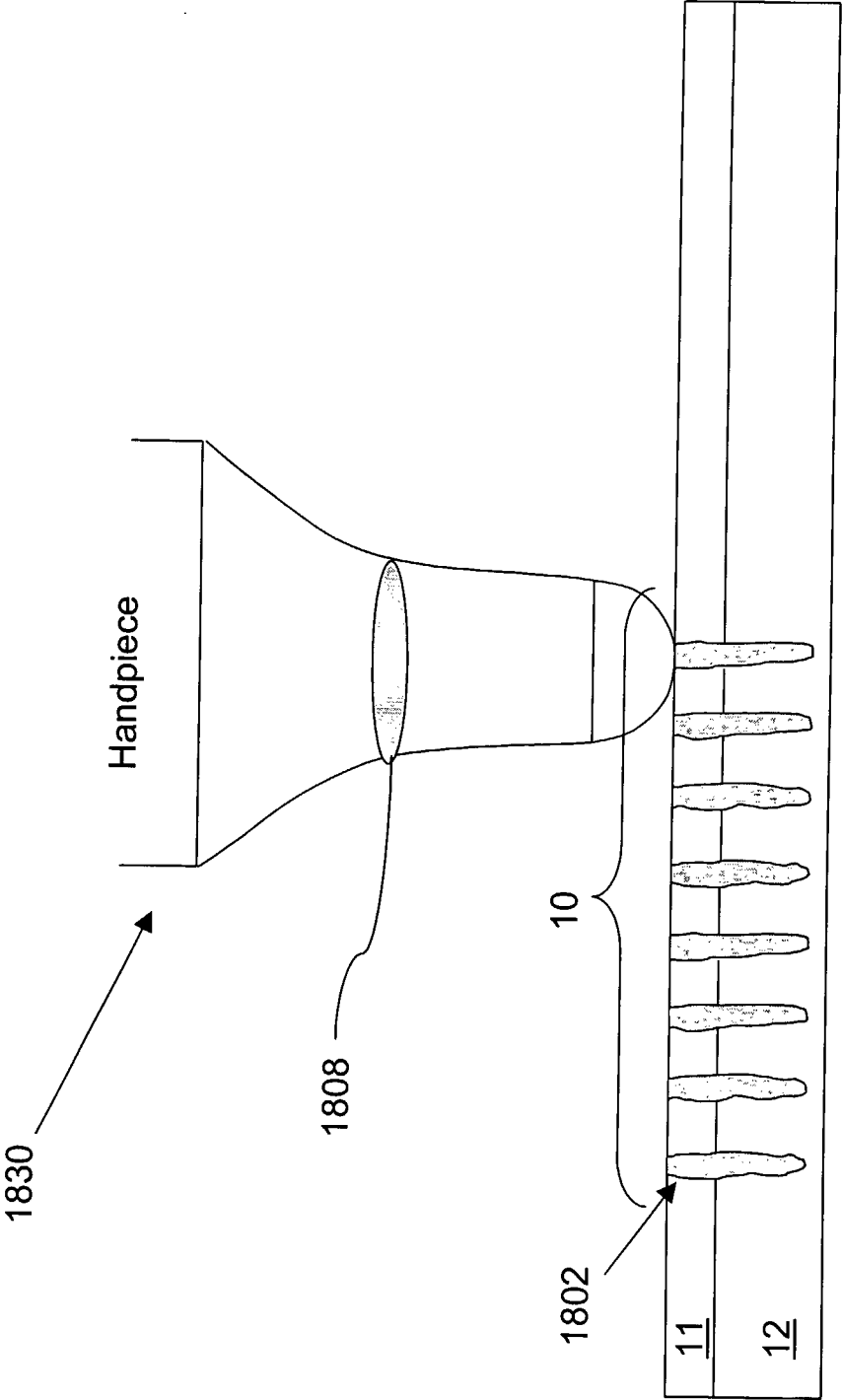
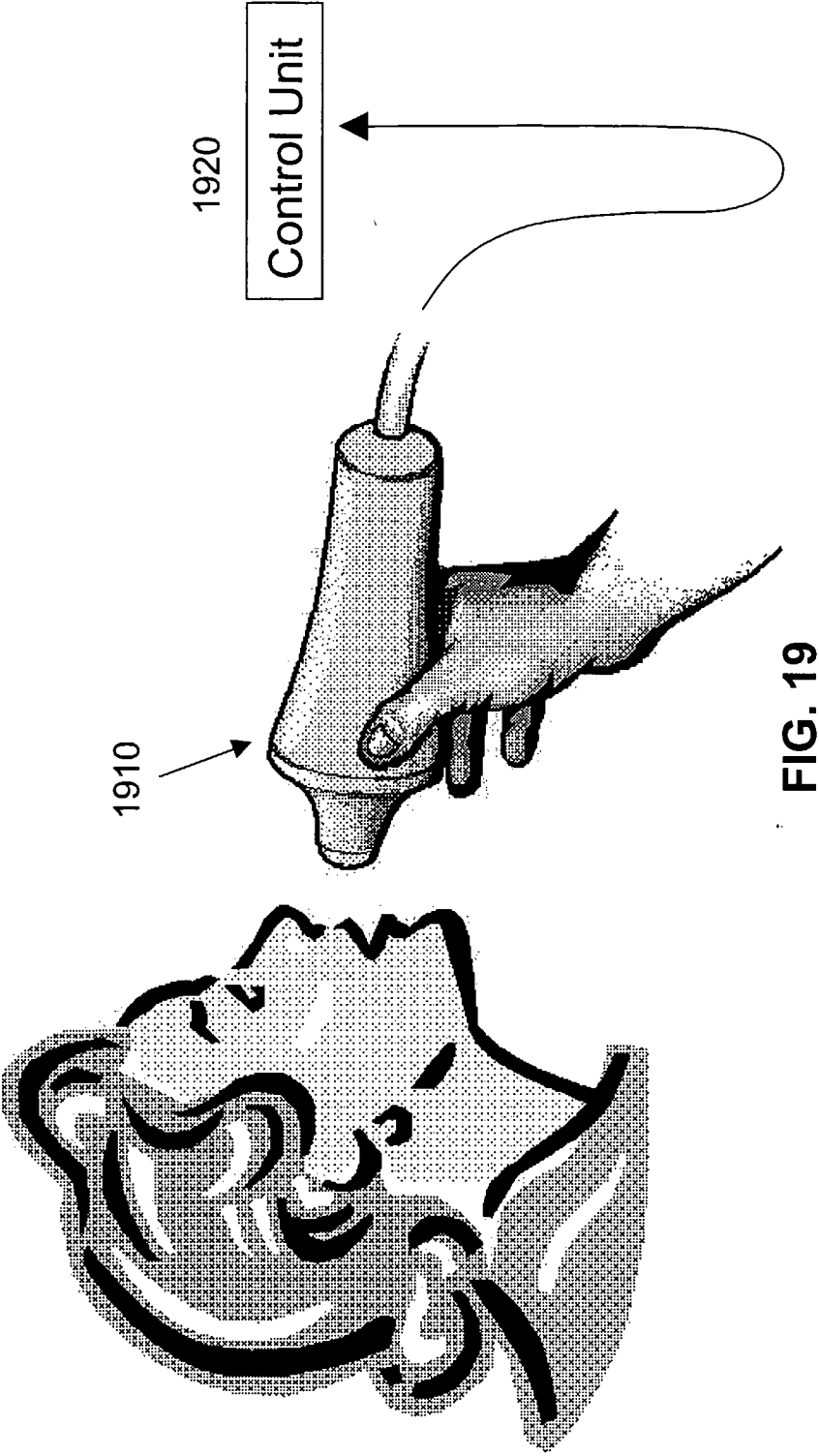


FIG. 18



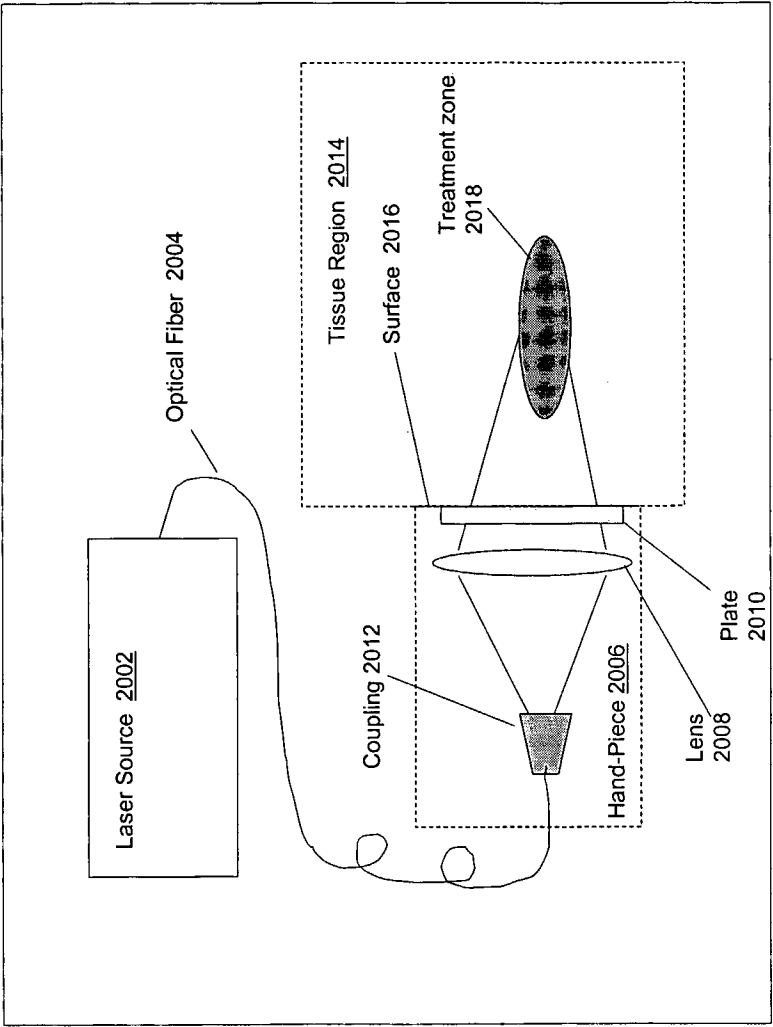


Fig. 20

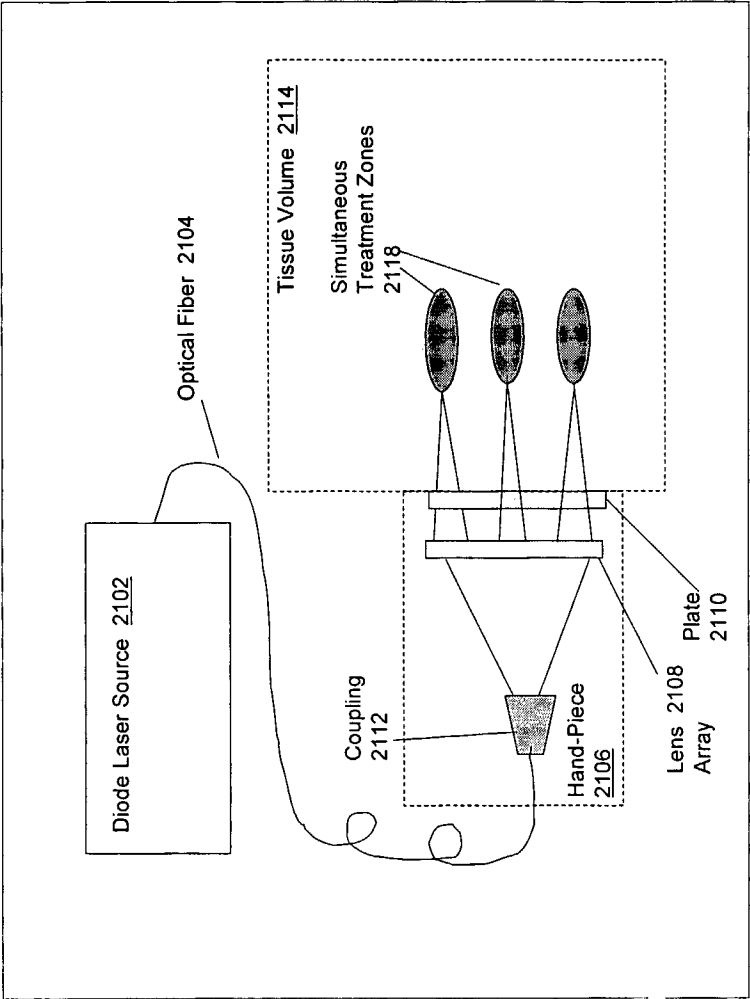


Fig. 21a



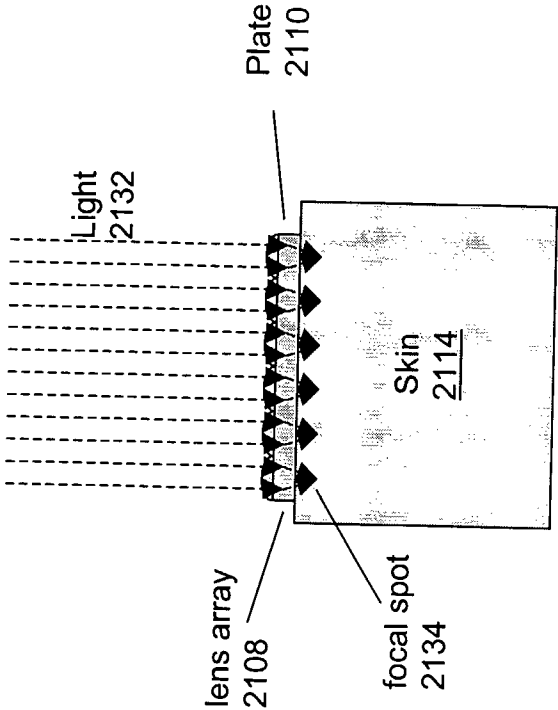


Fig. 21b

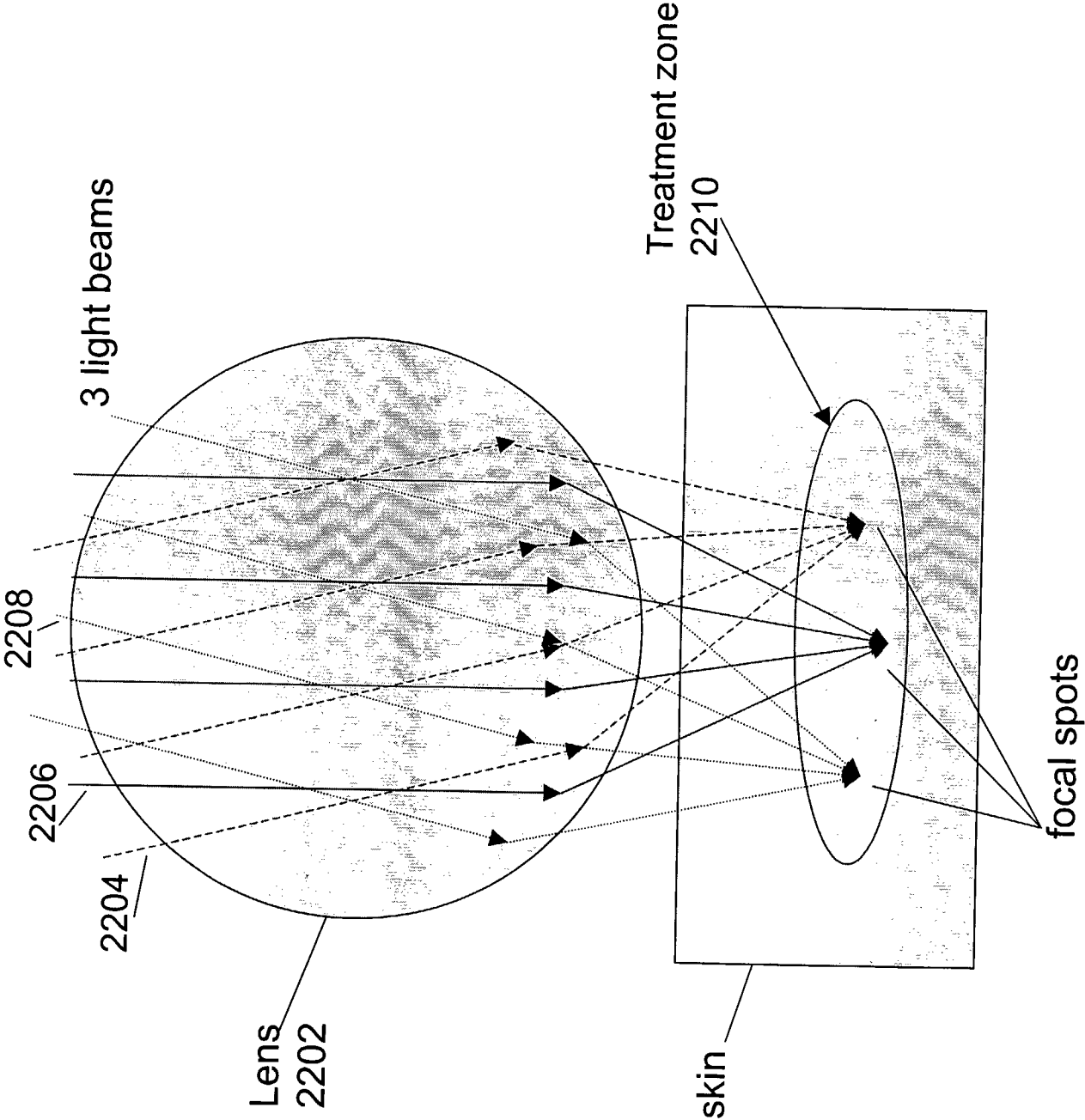


Fig. 22

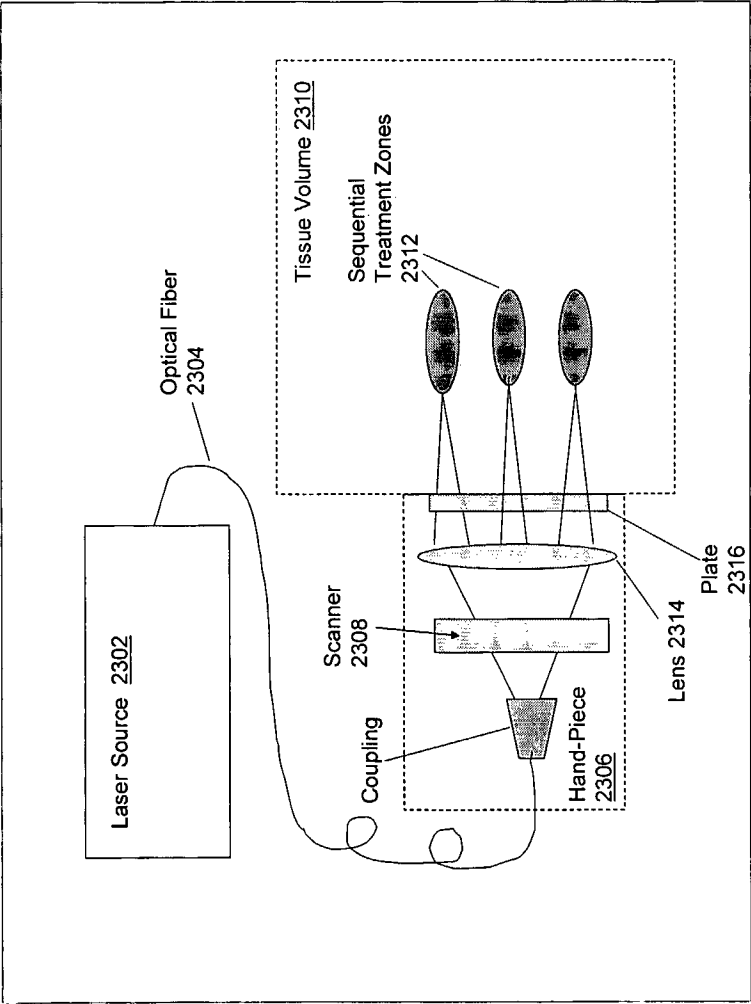


Fig. 23

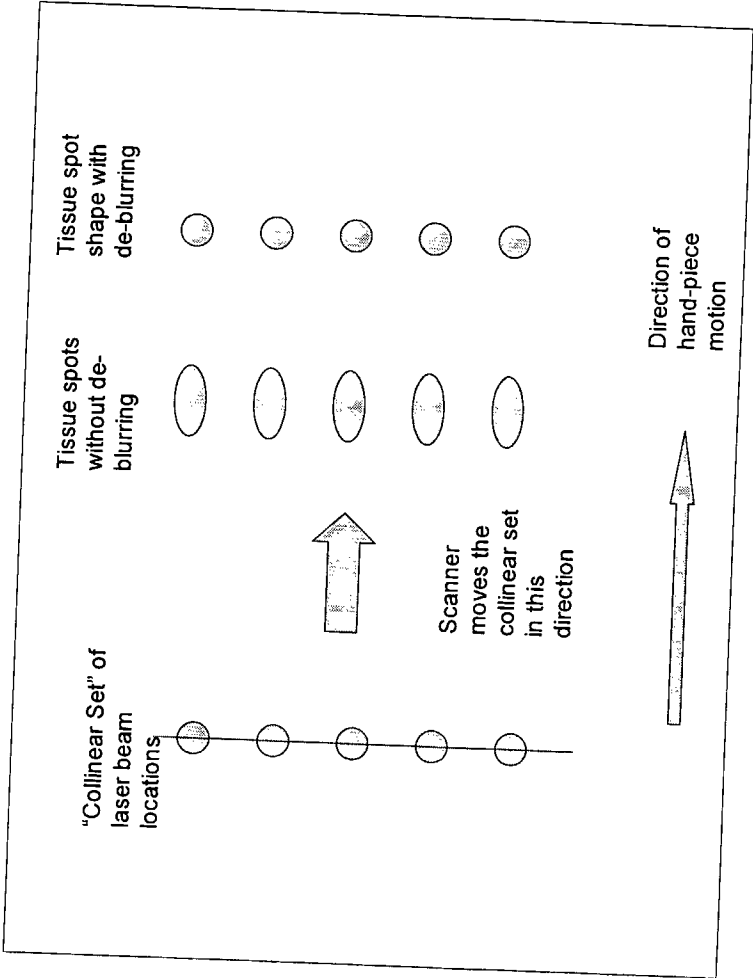


Fig. 24

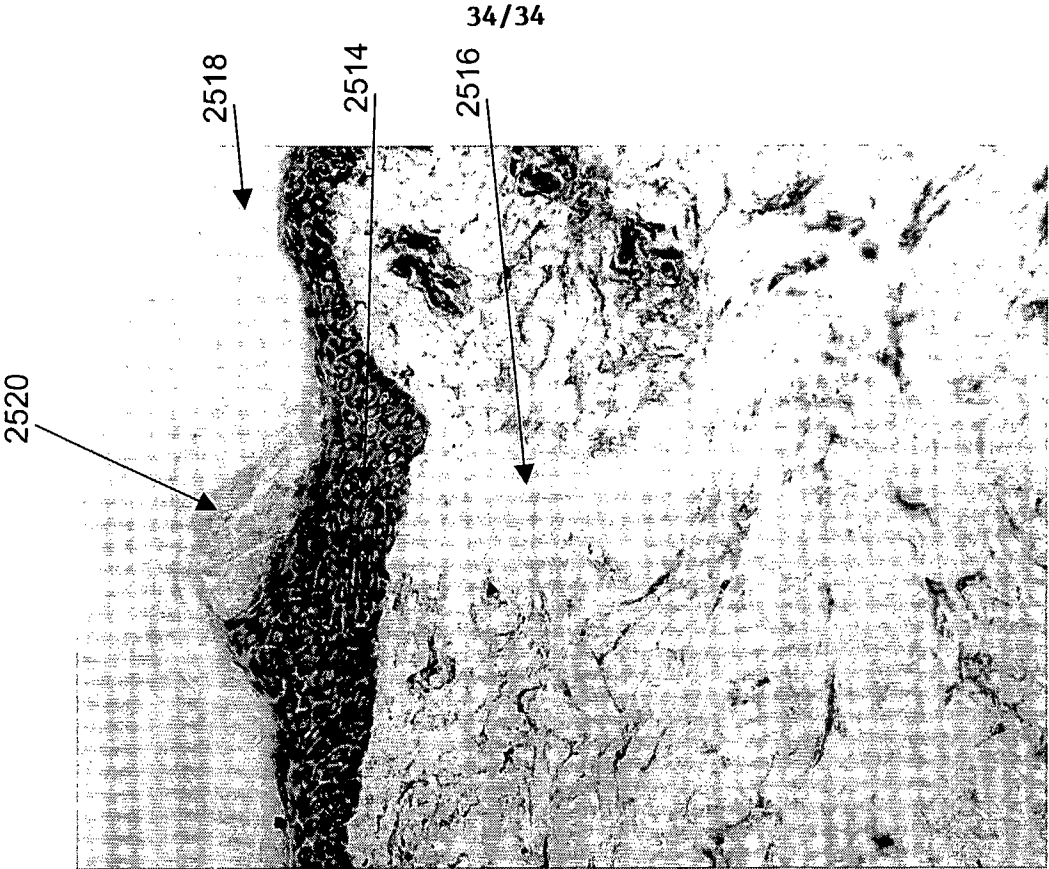


Fig. 25b

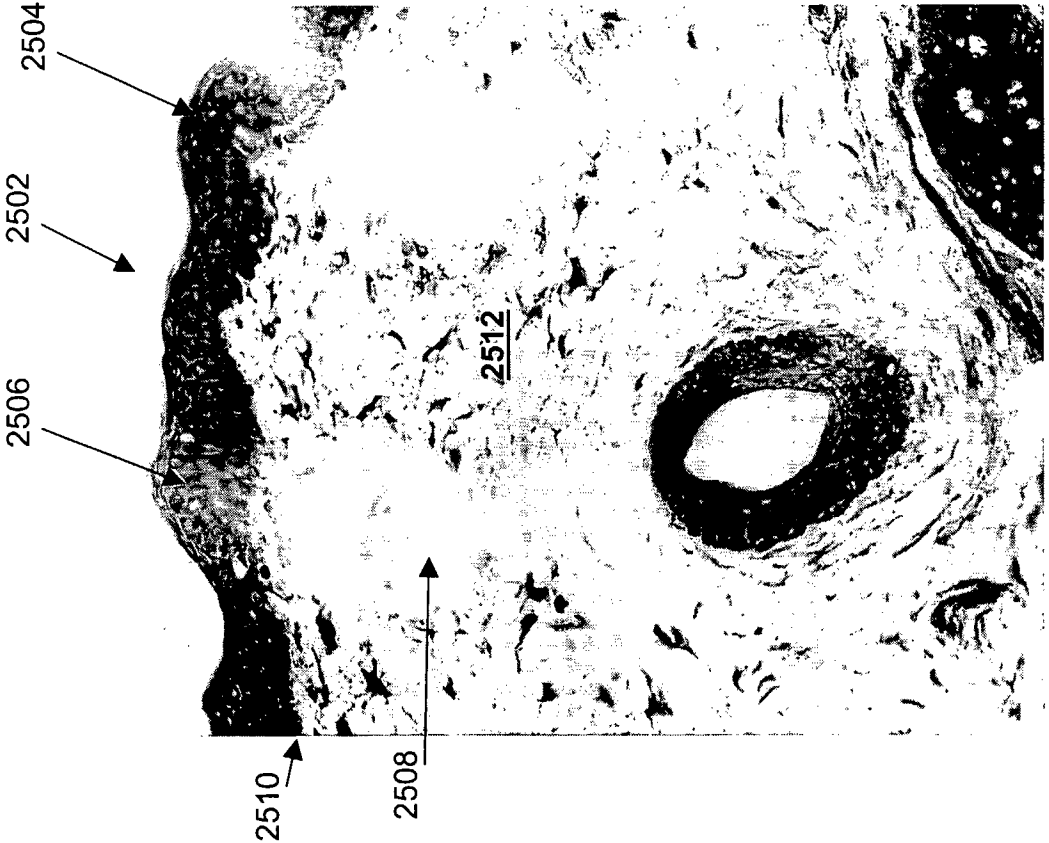


Fig. 25a

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61B18/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No                            |
|------------|---|---|
| X          | US 6 537 270 B1 (SCHROEDER ECKHARD ET AL)<br>25 March 2003 (2003-03-25)<br><br>abstract; figure 1<br>column 2, line 22 - line 29<br>column 2, line 42 - column 5, line 46<br>column 5, line 66 - column 6, line 45<br>-----         | 27-29,<br>31, 33,<br>34, 36,<br>40-45,<br>47-50 |
| X          | US 4 733 660 A (ITZKAN IRVING)<br>29 March 1988 (1988-03-29)<br><br>abstract; claims 1,4-6,9-12; figures 2,7<br>column 4, line 29 - column 5, line 56<br>column 7, line 20 - line 44<br>column 9, line 9 - line 51<br>-----<br>-/-- | 27-32,<br>35-46,<br>49-51,<br>53, 54            |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex

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Date of the actual completion of the international search

17 December 2004

Date of mailing of the international search report

29/12/2004

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/022389

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No                             |
|------------|---|--|
| X          | WO 99/27997 A (ESC MEDICAL SYSTEMS LTD ;<br>ECKHOUSE SHIMON (IL); FRIEDMAN MARK M<br>(IL);) 10 June 1999 (1999-06-10)<br><br>abstract; figures 3,5<br>page 2, line 8 - page 4, line 11<br>page 5, line 7 - page 6, line 23<br>----- | 28,29,<br>31,33,<br>35-38,<br>40-45,<br>47,49-52 |
| P,X        | WO 2004/037068 A (RELIANT TECHNOLOGIES<br>INC) 6 May 2004 (2004-05-06)<br>the whole document<br>-----   | 27-54  |

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/022389

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-26  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US2004/022389

| Patent document<br>cited in search report |    | Publication<br>date | Patent family<br>member(s) |               | Publication<br>date |
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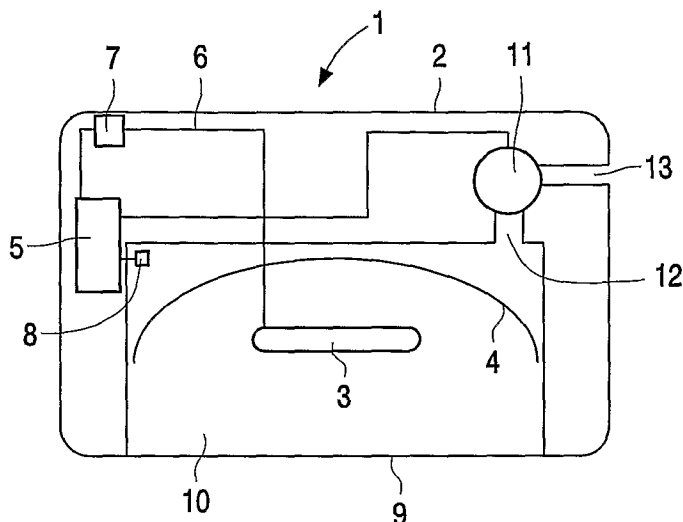
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[Continued on next page]

(54) Title: ELECTROMAGNETIC RADIATION DELIVERY APPARATUS



(57) Abstract: The present invention relates to a device for administering electromagnetic radiation to human tissue, in particular light to skin. The device comprises a treatment head with a recess (10) in which the light is emitted and in which the air pressure may be decreased by a pump (11). The device also comprises a pressure gauge (8) for measuring the pressure in the recess (10). Above a certain threshold value the device will not function, because this indicates an incorrect positioning of the device on the skin, which might cause harm to persons. By providing the pressure gauge (8), an operator may determine whether the positioning of the treatment head is correct. The device is advantageously automated in that the pressure gauge (8) is connected to control means (5) for controlling the source (3) of radiation.

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## Electromagnetic radiation delivery apparatus

The present invention relates to an electromagnetic radiation delivery apparatus for skin treatment, comprising a radiation delivery head having a source of electromagnetic radiation, an emission window which is optically coupled to the source of electromagnetic radiation and is able to emit the electromagnetic radiation, and a recess  
5 which is open on one side, and vacuum means for lowering a pressure inside the recess.

Document EP 1 285 600 A1 discloses an apparatus for laser depilation. The apparatus comprises a laser diode and a suction cap surrounding the laser diode. Air may be  
10 sucked out of the suction cap. The apparatus also comprises a control unit for controlling the sucking of air and the turning on and off of the laser diode in respect of time. The apparatus is intended for use as a depilation device.

The device known from the above mentioned European patent application, and in general many devices for treatment of body parts with the aid of electromagnetic radiation,  
15 are only operated by skilled personnel. This is due to the fact that it is readily possible to supply too much radiation to the body part to be treated. Furthermore, in the case of the known apparatus, it is possible to switch on the apparatus when it is not in a correct position. It is then possible that laser radiation is emitted which hits body parts not to be treated, such as eyes or skin parts of humans or animals nearby or even other objects susceptible to being  
20 damaged by the laser radiation. This is an unsafe and undesirable situation.

There is a general tendency towards more and more unskilled persons operating such devices. Hence there is an increasing need for apparatus that may be operated in a safe way, with a lowered risk of incorrect delivery of electromagnetic radiation.

25

An object of the present invention is to provide an apparatus of the abovementioned type, which can be operated more safely.

The object is achieved by an electromagnetic radiation delivery apparatus of the kind mentioned in the preamble of the main claim, characterized in that the apparatus

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further comprises a pressure gauge for measuring a pressure inside the recess. The pressure gauge offers a simple means enabling even an unskilled operator to check whether the apparatus is applied correctly to the body part or other surface to be treated. For only if the radiation delivery head with the recess is applied correctly, a vacuum, i.e. a pressure lower than ambient pressure, may be generated. The risk of inadvertently operating the delivery apparatus is thus lowered drastically.

The vacuum gauge may be a pressure meter combined with a display, a switch or other control means. A preferred embodiment of the apparatus according to the invention is further characterized by control means connected to the pressure gauge and to the source of electromagnetic radiation, wherein the control means are able to prevent the source of electromagnetic radiation from emitting electromagnetic radiation when the pressure measured by the pressure gauge is higher than a predetermined threshold value. By thus automating the operation of the apparatus the risk of incorrect use is lowered even further. The control means may be provided as for instance an electronic switch or shutter.

If an appropriate threshold value is set, it is not possible to operate the apparatus when the pressure is above that predetermined value. Consequently, even in the case of operation by unfit people, e.g. small children, the risk of causing harm or danger is reduced. It is to be noted that in the context of the present application, "measuring" a pressure means either determining an absolute value, or determining a relative value, e.g. with respect to the predetermined threshold value. In that case it is not necessary to determine the true pressure value, but only whether the pressure is above or below the threshold value.

The threshold value, i.e. the pressure value below which the apparatus should be turned off or is automatically turned off by the control means may be appropriately selected in accordance with the properties of the body part or surface to be treated. Advantageously, the threshold value is from 10 to 250 mbar below ambient pressure. If the body part or surface to be treated is smooth, flexible and compressible, a low pressure difference may be selected, e.g. 10 or 20 mbar below ambient pressure. If the surface to be treated is rough and incompressible, the threshold value should be much lower than ambient pressure, e.g. 200 mbar, in order to ensure a correct check on the position of the radiation delivery head, since there is the possibility of air leaking into the recess even when the delivery head is in the correct position. The power of the vacuum means should then be high enough for a sufficient pressure difference to be maintained in spite of the leaking in of air.

Of course the threshold value is dependent on the ambient pressure, which means that e.g. in an area of low pressure or at a high altitude, the threshold value is

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correspondingly lower than the threshold value in an area of high pressure or at sea level. Generally, the threshold value depends on the ambient pressure and may be expressed as a pressure difference with ambient pressure. In the presently preferred embodiment it is possible to define the threshold value as a (negative) pressure difference with ambient

5 pressure of between 10 and 250 mbar.

Preferably, during a period of time in which the measured pressure inside the recess is below the threshold value, the control means are able to prevent the electromagnetic radiation source from emitting electromagnetic radiation above a predetermined maximum amount of energy. By allowing only a certain maximum amount of energy to be emitted

10 during a session, overexposure of the skin, with possible (increased) discomfort or injury may be avoided. Moreover, there will be no more uncertainty whether or not a certain part of the skin received radiation.

Another possible criterion in determining the threshold value, or in other words the pressure difference with ambient pressure, is the fact that the relatively low

15 pressure (or high pressure difference) "sucks" the body part, in particular the skin, towards the electromagnetic radiation. Not only offers this the possibility of a controlled distance between the source of electromagnetic radiation and the body part or surface to be treated, but in the case of skin and other body parts, it also offers the advantage that the lower pressure improves the properties of those body parts for receiving radiation and responding

20 thereto, or it may reduce unwanted side effects, as is known in the prior art.

Since the electromagnetic radiation which is delivered to the body part or surface to be treated affects said body part or surface, it may be important to limit the total amount of supplied radiation. In a preferred embodiment, the control means are able to prevent re-operation of the apparatus, thereby ensuring that it is not possible to supply more

25 radiation energy than the predetermined maximum amount of energy without lifting the delivery head and hence breaking the vacuum.

Advantageously, the control means comprise a shutter that is able to prevent emission of the electromagnetic radiation. Such a shutter may take any desired form, e.g. an electro-optical shutter, a mechanical shutter, a switchable mirror etc. An advantage of the

30 presence of such a shutter is that the source of electromagnetic radiation need not be switched off when the apparatus is not to emit radiation. For many sources of electromagnetic radiation this is beneficial to the lifetime of the source. However, if frequent switching on and off of the source of electromagnetic radiation does not substantially shorten the lifetime

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of the source, it is also possible for the control means to simply switch the power source of the source of electromagnetic radiation, for example in the case of LED's.

In a preferred embodiment, an emission window is present in the recess. The term "emission window" relates to an area of the radiation delivery head through which electromagnetic radiation is emitted. It may come in the form of e.g. a piece of material that is transparent to the electromagnetic radiation to be emitted, e.g. glass in the case of optical light. However, it may also mean an open side of a cavity which is not covered by any material, e.g. an exit end of a tube. An advantage of an emission window being present in the recess is that when the recess is deemed to be positioned correctly, the emission window is automatically positioned correctly as well. In most cases, one emission window is present. However, it is to be noted that it is also possible for a plurality of emission windows to be present.

It is also possible for a plurality of recesses to be present. It may be contemplated that a number of small recesses is present in the form of a number of holes around the emission window. If all holes are positioned correctly, this too is a safe indication that the delivery apparatus is positioned correctly. However, preferably, a recess surrounds the emission window. This is a slightly more general instance of the case in which the emission window is present in the recess. If the recess surrounds the emission window, then an appropriate underpressure in the recess guarantees a correct positioning of the emission window. In this case the recess may come in the form of a groove around the emission window. In this way it is possible to have different shapes for the recess and the emission window. This offers advantages if the radiation is preferably supplied in a circular pattern, e.g. for homogeneity reasons, whereas a different part of the surface surrounding the part which is treated should not receive radiation. This part may of course have a different shape.

Preferably, the recess comprises a circumferential edge. In this way it is relatively simple to visually check the correct positioning by inspecting the circumferential edge.

Advantageously, the circumferential edge is flexibly deformable. This embodiment allows adaptation to a body part or surface not exactly matching the plane of the emission window or recess. Although it is possible to use a non-deformable delivery head, and to make use of the deformability of the body part or a surface to be treated, a flexibly deformable circumferential edge offers the advantage that the pressure exerted on the body part or surface differs less.

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If the emission window is in the form of a transparent piece of material, this piece of material may be used to exert pressure on the body part or surface to be treated. In this case, in particular in the case of skin, the bloodstream through said body part may be affected. For instance in the case of photo hair removal, it is advantageous if the blood  
5 circulation is reduced in the tissue being treated, because then there will be less absorption of radiation by tissue parts other than the intended parts (chromophores, hair follicles). Besides, risks of possible side-effects of the treatment are reduced.

The flexibly deformable circumferential edge may be designed as a rim of resilient material such as rubber. Any other flexibly deformable material or construction is  
10 also possible.

In an advantageous embodiment, the circumferential edge lies on a plane surface, on a concave surface or on a convex surface. With these simple geometries, most body parts or other surfaces to be treated can be treated efficiently. Plane surfaces may be used for treating e.g. artificial objects or small areas of large and hence relatively flat body  
15 parts such as legs. A concave surface for the circumferential edge may be useful when treating a convex body part, e.g. a relatively small body part such as a finger or other, strongly curved body parts such as a nose. A convex surface for the circumferential edge is advantageous for the treatment of more or less concave surfaces, such as for the depilation of arm pits. In specific cases other surfaces for the circumferential edge may be even more  
20 advantageous.

In a preferred embodiment of the apparatus according to the invention, the electromagnetic radiation comprises infrared radiation, visible optical radiation or ultraviolet radiation. For the purpose of the present application, infrared radiation, visible optical radiation and ultraviolet radiation will be referred to as "optical radiation". Optical radiation  
25 is a part of the electromagnetic spectrum which is most often used for the treatment of body parts, especially by non-skilled or other private persons. In principle, however, it would be possible to use other types of electromagnetic radiation, e.g. microwave radiation or x-rays.

The preferred electromagnetic radiation according to the invention (optical radiation) covers treatments by means of heat (infrared radiation) for treatment of muscle  
30 pain, depilation, treatment of hyperbilirubinaemia, etc. by means of visible optical radiation, and artificial tanning and treatment of various skin disorders, such as vitiligo and psoriasis. Although some treatments may be performed by non-skilled or non-professional personnel, such as tanning and depilation, in many cases it may be preferable to have professional skilled personnel perform the treatment. Nevertheless, also in the case of professional



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personnel, the improved safety and other advantageous features of the apparatus according to the invention are valid.

Throughout the application the words "body part" and "surface to be treated" relate to any human tissue surface susceptible to a treatment by means of electromagnetic radiation. In particular this relates to skin (human skin). In general, however, any other treatable surface may be contemplated, e.g. in the field of materials research, curing of material. However, the invention has special advantages when used in relation to treatment of humans or animals, since the risks of inadvertent injury through accidents etc. are much reduced.

10 In the apparatus according to the present invention, the source of electromagnetic radiation may be comprised in the radiation delivery head. This means that e.g. a light source such as a LED or a high-pressure gas discharge lamp is built into the radiation delivery head. However, in an advantageous embodiment, the source of electromagnetic radiation comprises electromagnetic radiation generating means and  
15 electromagnetic radiation guiding means optically connected thereto. The presence of an electromagnetic radiation generating means and electromagnetic radiation guiding means offers the possibility of separation of these two functions. This means that a complex, large and heavy electromagnetic radiation generating means, such as a high power laser, may be present at a certain distance from the delivery head. The delivery head, which eventually  
20 emits the radiation generated by the electromagnetic radiation generating means is optically connected to the electromagnetic radiation guiding means so that the latter can guide the electromagnetic radiation to the radiation delivery head, and eventually to the emission window. This allows a relatively small and light-weight delivery head, which greatly improves the ease of use of the apparatus.

25 In an advantageous embodiment, the electromagnetic radiation guiding means comprise a mirror, a hollow electromagnetic radiation guide or an optical fibre. The person skilled in the art will know how to select the appropriate guiding means. E.g. in the case of a laser, an optical fiber may be the guiding means of choice. A mirror may be used in the case where a laser is the electromagnetic radiation generating means and the laser beam is used to  
30 scan a certain area to be treated. This allows said area to be illuminated homogeneously by the laser beam without the operator having to move the radiation delivery head. This greatly improves the efficacy and homogeneity of the treatment.

Advantageously, the source of electromagnetic radiation comprises a laser, a flash lamp, a LED, a gas discharge lamp or an incandescent lamp. These sources of

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electromagnetic radiation have proved to be efficient and useful in a wide variety of possible uses of the apparatus according to the invention. They come in a large variety of wavelengths, powers etc. Nevertheless, in particular cases, other sources may be used also, such as x-ray sources.

5

Embodiments of an electromagnetic radiation delivery apparatus in accordance with the invention will be described in detail hereafter with reference to the appended drawing, in which:

10 Figs. 1a, 1b show a schematic cross-sectional view, bottom view, respectively, of a first embodiment of the device according to the invention,

Figs. 2a, 2b show a schematic cross-sectional view, bottom view, respectively, of a second embodiment of the device according to the invention, and

15 Figs. 3a, 3b show a schematic cross-sectional view of a third embodiment, applied correctly and incorrectly, respectively.

Figs. 1a,b show a schematic cross-sectional view, bottom view, respectively of a first embodiment of a device 1 according to the invention. Herein, 2 is a housing for a lamp 20 3 and a reflector 4. Control means 5 are connected to lamp 3 via a supply cable 6, and to switch 7, and to vacuum gauge 8. An emission window 9 borders a recess 10. A vacuum pump 11 is connected to vacuum outlet 12 and to exhaust pipe 13. The device 1 comprises a treatment head which for its operation only requires a connection to the mains, or possibly only some kind of battery or other power source of its own.

25 The housing 2 may be made of any kind of material. Preferably a material is used which is compatible with human skin, i.e. a non-toxic, non-allergenic material, such as many plastics or metals like aluminum or steel. Optionally the materials may be coated.

The housing 1 houses a lamp 3, which may be e.g. a flash lamp, a halogen incandescent lamp or a laser, without excluding other kinds of light source. Here, as in the 30 whole of the application, "light" refers to the part of the electromagnetic spectrum having wavelengths between about 300 nm and 1500 nm, i.e. ultraviolet to (medium wave) infrared radiation. The spectrum may be continuous or monochromatic, and the radiation may be emitted continuously or intermittently, as e.g. in a pulsed laser or a flash lamp.

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Control means 5 control the operation of the lamp 3 via supply cable 6. Supply cable 6 may be a combination of an ordinary two-core electrical cable and a data cable or any other appropriate cable known in the art. Control means 5 may be embodied as ROM, a computer etc. A separate switch 7 may be supplied for actually switching the lamp 3 on and off.

The control means are also connected to a vacuum gauge 8. When the pressure signal of the vacuum gauge is such that it indicates too low a pressure difference, i.e. too high an absolute pressure, the control means either switch off or prevent the switching on of the lamp 2, or send a signal to the switch 7 to the same effect.

The vacuum gauge 8 measures the pressure inside a recess 10. The pressure inside the recess 10 is made to decrease by a pump 11, which sucks away the air inside the recess through a vacuum outlet 12 and an exhaust tube 13, which is connected to the environment. The power of the pump should preferably be selected such that the pressure inside the recess 10 drops to a value that is between about 10 and 250 mbar lower than ambient pressure. Depending on altitude and air pressure, this may correspond to an absolute pressure of between 1020 mbar and about say 600 mbar. The pressure difference should preferably not be so large that it causes discomfort to the person being treated. To this end, and also in order to be able to remove the treatment head from the skin, a valve for venting the recess is advantageously provided, either in the recess or in the vacuum means. It is to be noted that it is the pressure difference with ambient pressure which determines whether the lamp is allowed to be switched on, and also whether said safety valve should open.

The pump 11 is advantageously connected to the control means 5 in order to be switched on and off when desired. Even more advantageously, the control means may set the power of the pump 11 in order to adapt to changing ambient conditions.

The vacuum gauge 8 may be some kind of pressure difference meter which gives off an analogue or digital signal, or an absolute pressure meter. In the latter case, a desired threshold value (i.e. a value of the pressure above which the lamp should not be turned on) may be set in the pressure meter. Another possibility is that the pressure meter supplies a pressure value signal to the control means 5, which may evaluate the signal in order to decide whether or not to switch the lamp on or off.

The light from the lamp 3 is reflected by a reflector 4 towards an emission window 9, which in this case is nothing more than an opening in the housing. The emission window 9 is a connection between the recess 10, or hollow space inside the housing 2, and the environment. When the device 1 is placed correctly on the skin, the recess will be sealed

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tightly by the skin, so that no ambient air will enter the recess. In this case it is easy for the pump 11 to reach a sufficiently low pressure value inside the recess, i.e. below the threshold value. On the other hand, if the device is not placed correctly, air will leak into the recess, destroying the vacuum seal, and preventing the pressure inside the recess from dropping sufficiently. This will be elucidated further in the discussion of Figure 3.

Another advantage of the sucking away of air from the recess is that any odours, debris etc. that are formed during or because of the treatment, will be sucked away as well. E.g., waste gases or cut hairs will be removed from the debris. To that end, the pump means and/or the vacuum outlet may be provided with a suitable filter. This will prevent damage to or soiling of the pump, and will ensure safe and clean removal of waste and a pleasant smell of the exhaust gas.

In this case the treatment head is the device. In other cases some parts of the device may be external to the treatment head. In particular, the treatment head is considered the part of the device with the recess and the emission window. The device as a whole consists in that case of the treatment head and the external parts, e.g. a vacuum pump and control means.

The control means 5 may be adjusted to allow only a certain amount of energy to be emitted during a single "session". In this respect, a session indicates the positioning of the treatment head on a certain spot of the skin, decreasing the air pressure to an operative value below threshold, emitting radiation, and increasing the air pressure to above threshold, in particular to ambient pressure. By allowing only a certain maximum amount of energy to be emitted during a session, overexposure of the skin, with possible (increased) discomfort or injury may be avoided. There will be no more uncertainty whether or not a certain part of the skin received radiation. The operator of the device will then be forced to lift the device and apply it again to the skin. He can then e.g. select a different area for the next treatment to avoid injury to the skin. Alternatively, e.g. in the case of treatment of deeper (skin) tissue layers, he can again apply the device to the same area of the skin, but preferably only after some time has elapsed, in order to allow the skin or other tissue parts to cool. A delay time of about 1 second or more is sufficient in most cases. Advantageously, the control means comprises means for setting a delay time, during which delay time the device is incapable of emitting radiation.

Figs. 2a, b show a cross-sectional view, bottom view, respectively, of a second embodiment of a device according to the invention. Here, as in all drawings, similar parts will be denoted by the same reference numerals. The housing 2 again comprises a light

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source 3 and a reflector 4. The light source is connected to a supply cable 5. The housing comprises a circumferential recess 14 connected to a vacuum gauge 8 and a vacuum outlet 12, an emission window 9 and a circumferential edge 15. In this second embodiment, the lamp 3 is not located in the space in which the pressure will be decreased, but instead a  
5 separate space is sealed off by an emission window 9. The emission window 9 is a window of glass, a plastic, quartz etc. It may be treated to act as a filter of the radiation, e.g. by coloring the material. It may be advantageous to close off the space for the lamp, e.g. because sometimes the lamp will get very hot, produce ozone, etc., which may be dangerous to humans.

10 The second embodiment uses a circumferential recess 14 in order to check a correct position of the device 1 on the skin. A pressure value in the circumferential recess 14 which is lower than the threshold value will ensure a correct position of the device because the skin is a continuous surface.

In this second embodiment only a vacuum gauge 8 is present in the device (or  
15 treatment head) 1. Other parts like a pump, control means and a switch are external to the treatment head, and are connected to the relevant parts in the treatment head by means of the cable 6 and/or the vacuum outlet 12. This ensures a more light-weight and handy treatment head. It is to be noted that the vacuum gauge 8 could also be located outside the treatment head, e.g. inside the vacuum outlet near the external pump. However, it is safer to measure  
20 the pressure at the exact location where it is to be known, to prevent the risk of e.g. a blocking of the vacuum outlet between the (circumferential) recess and the vacuum gauge 8. This would simulate an incorrect actual pressure inside the recess, and lead to possibly dangerous situations.

In this case too, it is possible to ensure safe and efficient removal of waste gas,  
25 even though the circumferential recess is not connected to the space for the lamp. As soon as a correct low pressure is reached, the pump may be switched off, and the treatment may begin. After finishing the treatment, the treatment head will be lifted. At that moment, the vacuum will be broken, and the pressure will start to rise. This triggers the vacuum gauge 8 and the control means, which will switch on the pump. The pump will then suck away the  
30 gases etc. through the circumferential edge 15.

The circumferential edge 15 is simply a more "angular" version of the corresponding feature in the first embodiment. Although it might possibly be somewhat less comfortable for the person to be treated, it does ensure a safer visual check whether the device is positioned correctly on the skin. It suffices to visually check whether the edge 15

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engages the skin. In a more rounded off version, this is less reliable because even in a correct position the edge which is visible from the outside need not engage the skin. It is only the lower, invisible part of the edge which must engage the skin.

Figs. 3a, b show schematic cross-sectional views of a third embodiment of a device 1 in a correct position and an incorrect position, respectively. The device comprises a housing 2 with a recess and a vacuum outlet 12. The source of electromagnetic radiation is a fiber bundle 16 splitting up into a plurality of individual fibers 17 that each emit a bundle of radiation 18. In this case that part of the device which emits light into the recess, in particular the light emitting ends of the (optical) fibers, is considered to be the light source.

In this third embodiment even the vacuum gauge and the actual electromagnetic radiation (or "light") generating means are absent from the actual treatment head, in order for the latter to have minimum weight and dimensions. Of course, the light generating means will be optically coupled to the treatment head. E.g. the light generating means such as a laser is located in direct contact with an opposite end of the fiber bundle 16. An important advantage of this embodiment is the absence of any electrical parts in the treatment head proper, which is very safe for humans.

In Fig. 3a the treatment head is positioned correctly, i.e. such that no ambient air can enter the recess. The pump (not shown) will have no difficulty in decreasing the air pressure in the recess to a value below the threshold value. The device will work safely and can be switched on.

As can be seen in Fig. 3a, the low air pressure inside the recess may also be used to draw the skin into the recess, at least for a certain distance. This will cause the blood circulation to change favorably. It will also decrease the distance to the light sources to a certain degree.

In Fig. 3b an example is given of an incorrectly positioned device. Outside air can leak into the recess as indicated by the arrows, which prevents that the pump decreases the pressure in the recess sufficiently. Therefore the device will not be switched on, for it would not work safely because radiation might escape. Also in the case that the device is placed on a fold or other uneven part of the skin, a correct vacuum cannot be obtained, and the device will not be switched on. Of course, when during correct operation the position suddenly becomes incorrect, for instance because of an unexpected movement by the person being treated, such that the vacuum "seal" of the recess is broken, the rising air pressure will also cause the device to be turned off.

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## CLAIMS:

1. An electromagnetic radiation delivery apparatus for skin treatment, comprising a radiation delivery head having a source of electromagnetic radiation, an emission window which is optically coupled to the source of electromagnetic radiation and is able to emit the electromagnetic radiation, and a recess which is open on one side, and vacuum means for  
5 lowering a pressure inside the recess, characterized in that the apparatus further comprises a pressure gauge for measuring a pressure inside the recess.
2. An apparatus according to claim 1, further characterized by control means connected to the pressure gauge and to the source of electromagnetic radiation, wherein the  
10 control means are able to prevent the source of electromagnetic radiation from emitting electromagnetic radiation when the pressure measured by the pressure gauge is higher than a predetermined threshold value.
3. An apparatus according to claim 2, characterized in that the threshold value is  
15 from 10 to 250 mbar below ambient pressure.
4. An apparatus according to claim 2 or 3, characterized in that, during a period of time in which the measured pressure inside the recess is below the threshold value, the control means prevent the electromagnetic radiation source from emitting electromagnetic  
20 radiation above a predetermined maximum amount of energy.
5. An apparatus according to any of claims 2-4, characterized in that the control means comprise a shutter that is able to prevent emission of the electromagnetic radiation.
- 25 6. An apparatus according to any of the preceding claims, characterized in that an emission window is present in the recess.
7. An apparatus according to any of the preceding claims, characterized in that a recess surrounds the emission window.

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8. An apparatus according to any of the preceding claims, characterized in that the recess comprises a circumferential edge.
- 5 9. An apparatus according to claim 8, characterized in that the circumferential edge is flexibly deformable.
10. An apparatus according to claim 8 or 9, characterized in that the circumferential edge lies on a plane surface, on a concave surface or on a convex surface.
- 10 11. An apparatus according to one or more of the preceding claims, characterized in that the electromagnetic radiation comprises infrared radiation, visible optical radiation or ultraviolet radiation.
- 15 12. An apparatus according to one or more of the preceding claims, characterized in that the source of electromagnetic radiation comprises electromagnetic radiation generating means and electromagnetic radiation guiding means optically connected thereto.
- 20 13. An apparatus according to claim 12, characterized in that the electromagnetic radiation guiding means comprise a mirror, a hollow electromagnetic radiation guide or an optical fiber.
- 25 14. An apparatus according to one or more of the preceding claims, characterized in that the source of electromagnetic radiation comprises a laser, a flash lamp, a LED, a gas discharge lamp or an incandescent lamp.



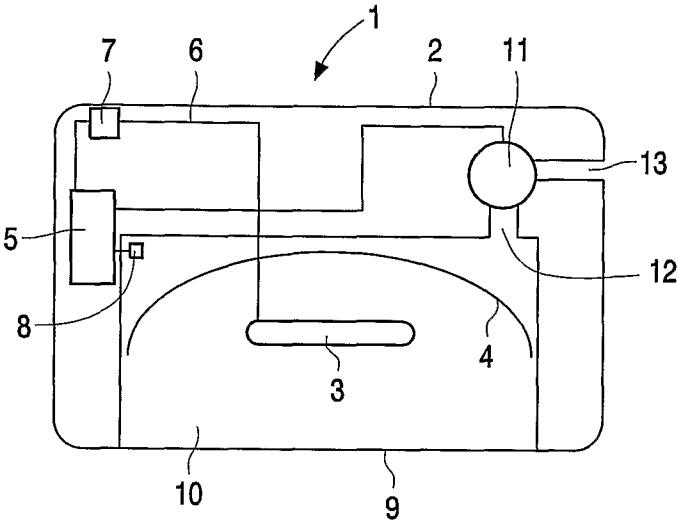


FIG. 1a

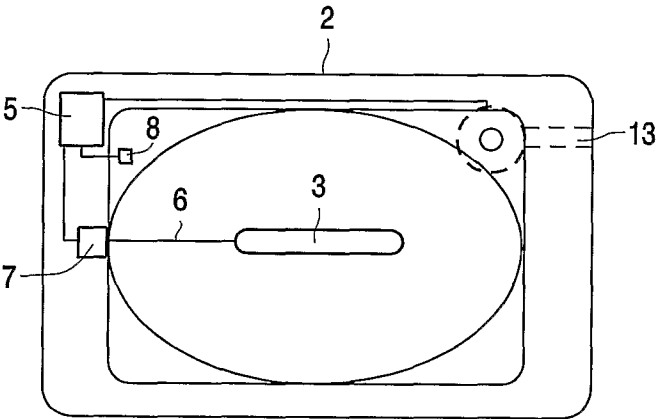


FIG. 1b

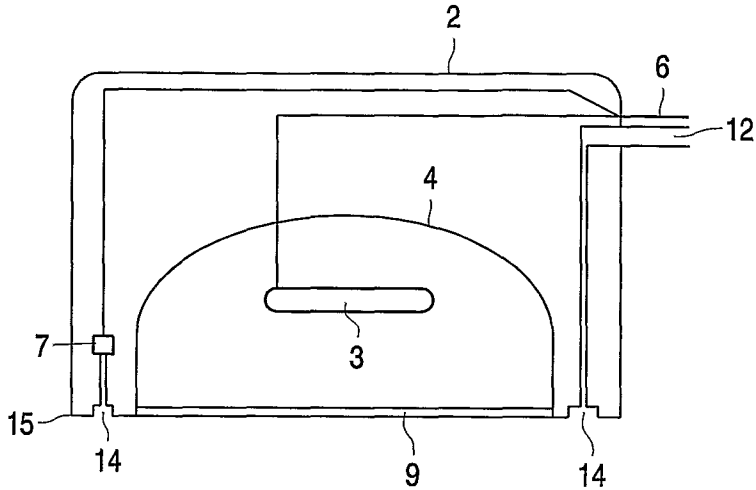


FIG. 2a

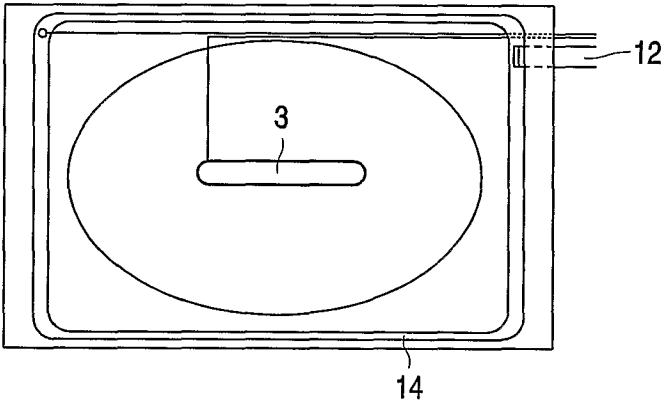


FIG. 2b

3/3

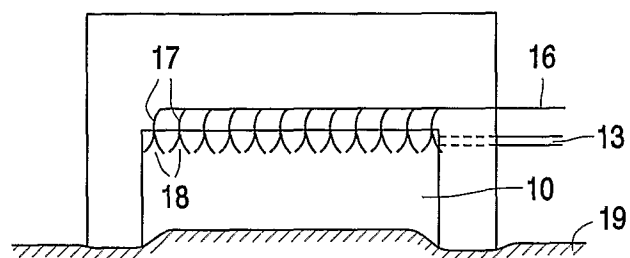


FIG. 3a

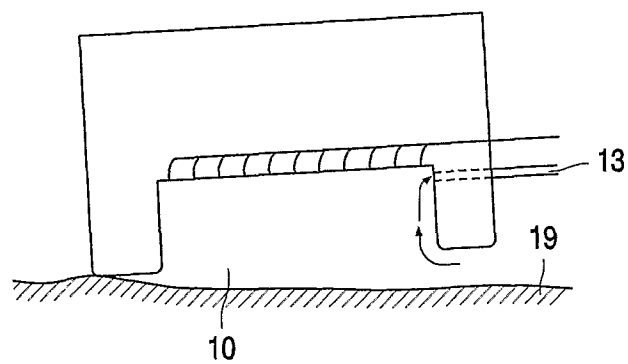


FIG. 3b

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61B18/20 A61N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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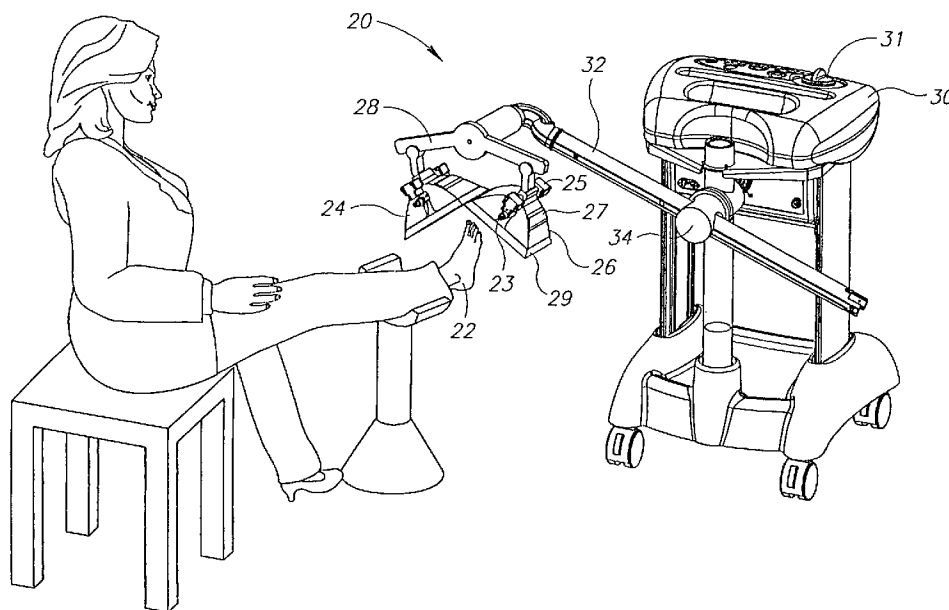
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(54) Title: PHOTOTHERAPEUTIC TREATMENT OF SKIN CONDITIONS



(57) Abstract: A method for treating an inflammation in skin of a patient includes irradiating the skin with infrared (IR) radiation in a first wavelength band and with violet/blue light in a second wavelength band.

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PHOTOTHERAPEUTIC TREATMENT OF SKIN CONDITIONSCROSS-REFERENCE TO RELATED APPLICATIONS

5           This application is a continuation-in-part application of U.S. Patent Application  
No. 10/674,313 filed September 30, 2003 which is a continuation-in-part application  
of U.S. Patent Application Serial No. 10/366,452, filed February 13, 2003, and of  
U.S. Patent Application No. 10/098,592, filed March 18, 2002. These applications  
are continuations-in-part of U.S. Patent Application No. 10/007,702, filed December  
10   10, 2001, which is a continuation-in-part of U.S. Patent Application No. 09/756,130,  
filed January 9, 2001, which is a continuation-in-part of PCT Patent Application No.  
PCT/IL99/00374, filed July 7, 1999. The disclosures of all these related applications  
are incorporated herein by reference.

15

FIELD OF THE INVENTION

The present invention relates generally to skin phototherapy, and specifically  
to treatment of skin inflammations.

20

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BACKGROUND OF THE INVENTION

It is known in the art to use violet/blue light, in the spectral range between 405 and 450 nm, for treatment of skin conditions, such as acne vulgaris. The *P. Acnes* bacteria, which are the cause of acne skin lesions, produce porphyrins, which become toxic in the presence of light in this range. This method of treating acne is described in the above-referenced related applications, as well as in an article by Elman et al., entitled "The Effective Treatment of Acne Vulgaris by a High-Intensity, Narrow Band 405-420 nm Light Source," *Journal of Cosmetic and Laser Therapy* 5 (2003), pages 111-116.

U.S. Patent 6,183,500, to Kohler, whose disclosure is incorporated herein by reference, describes a process and apparatus for the cosmetic treatment of acne vulgaris by irradiating the affected skin areas with light characterized by a combination of two emission spectra, one in a blue region and the other in a red region. The light is generated by low-pressure mercury discharge having two different spectra, one in the blue range from 400 to 450 nm, and the other in the red range from 580 to 659 nm.

The above-mentioned U.S. Patent Application 10/098,592 (published as US 2002/0173833) describes the use of violet/blue radiation in the range of 400-450 nm to reduce the level of extra-cellular pro-inflammatory cytokines. The inventors indicate that this cytokine-reducing effect may be useful not only in anti-inflammatory



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treatment of acne sites, but also in treating other inflammatory skin conditions, such as skin ulcers and cutaneous autoimmune diseases.

Shnitkind et al. describe a study into the therapeutic effect of blue light in a poster paper entitled, "Anti-Inflammatory Properties of Narrow Band Blue Light," presented at the Annual Meeting of the US Society of Investigative Dermatology (May, 2002), which is incorporated herein by reference. This study was conducted to investigate the effect of narrow band blue light on the inflammatory process in the presence and absence of cytokines and UVB radiation. (The release of cytokines from cutaneous cells is known to be important in the initiation and development of many inflammatory skin disorders.) The study showed that high-intensity, narrow band blue light has anti-inflammatory effect on keratinocytes by suppressing the cytokine-induced upregulation of IL-1alpha.

Infrared (IR) radiation sources, operating at around 890 nm, have been used to promote healing of different types of skin wounds. This use of IR radiation is described, for example, by Horwitz et al., in "Augmentation of Wound Healing Using Monochromatic Infrared Energy," *Advances in Wound Care* (January/February 1999), pages 35-40, which is incorporated herein by reference. The authors applied monochromatic IR radiation at 890 nm to recalcitrant dermal lesions, including venous ulcers, diabetic ulcers and a wound related to scleroderma. They note that the rate and quality of healing following IR irradiation may be related to local

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increases in nitric oxide (NO) concentration, which have been demonstrated to correlate with vasodilatory and anabolic responses.

### SUMMARY OF THE INVENTION

5

Embodiments of the present invention provide improved methods and apparatus for treatment of inflammatory skin conditions, by combined irradiation with violet/blue and infrared (IR) radiation. The present invention stems from the realization that swelling due to skin inflammations, such as ulcers, post-resurfacing and post-operative conditions, aging and other lesions, tends to reduce blood and/or lymphatic circulation in the vicinity of the inflammation. The impaired circulation, in turn, exacerbates the inflammatory condition and retards healing. The effectiveness of violet/blue light by itself in reducing levels of pro-inflammatory agents may thus be limited by inadequate circulation in the inflamed area. The addition of IR irradiation, as taught by the present invention, overcomes this limitation by enhancing circulation during the anti-inflammatory violet/blue light treatment.

There is therefore provided, in accordance with an embodiment of the present invention, a method for treating an inflammation in skin of a patient, including irradiating the skin with infrared (IR) radiation in a first wavelength band and with violet/blue light in a second wavelength band.

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Typically, the first wavelength band is selected to cause dilation of blood vessels in a vicinity of the inflammation, and irradiating the skin with the violet/blue light includes applying the violet/blue light to the inflammation while the blood vessels are dilated. Irradiating the skin may include irradiating the skin with the IR  
5 radiation and the violet/blue light simultaneously or sequentially.

In disclosed embodiments, the first wavelength band is in the range 800-980 nm, and the second wavelength band is in the range 405-450 nm. Typically, the first wavelength band is in the range 850-900 nm. In some embodiments, irradiating the  
10 skin includes irradiating the skin with at least 4 mW/cm<sup>2</sup> of the violet/blue light and at least 1 mW/cm<sup>2</sup> of the IR radiation, and typically with at least 20 mW/cm<sup>2</sup> of the violet/blue light and at least 8 mW/cm<sup>2</sup> of the IR radiation.

Typically, irradiating the skin includes irradiating the skin continuously for at  
15 least one minute. Alternatively, irradiating the skin includes irradiating the skin with pulsed radiation.

In a disclosed embodiment, irradiating the skin includes irradiating the skin using a single radiation source, which emits both the violet/blue light and the IR  
20 radiation, wherein the single radiation source includes a discharge lamp containing metal halide materials selected to radiate in the first and second wavelength bands. In another embodiment, irradiating the skin includes irradiating the skin using an array of solid-state radiation sources.

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Typically, irradiating the skin includes treating a condition selected from a group of conditions consisting of skin aging, ulcers, edema, rosacea, chronic cutaneous inflammatory conditions and acne. A medicated cream may be applied to

5 the skin in conjunction with irradiating the skin.

In one embodiment, irradiating the skin includes irradiating the skin using a radiation source that is in contact with the skin.

10 There is also provided, in accordance with an embodiment of the present invention, apparatus for treating an inflammation in skin of a patient, including at least one radiation source, which is adapted to irradiate the skin with infrared (IR) radiation in a first wavelength band and with violet/blue light in a second wavelength band.

15

In a disclosed embodiment, the at least one radiation source includes a single radiation source, which emits both the violet/blue light and the IR radiation. Typically, the single radiation source includes a discharge lamp containing metal halide materials selected to radiate in the first and second wavelength bands,

20 wherein the metal halide materials may include gallium and cesium halides.

In another embodiment, the at least one radiation source includes a plurality of radiation sources, and the apparatus includes an adjustable bracket, on which the

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radiation sources are mounted, so as to allow a relative angular orientation of the radiation sources to be adjusted. Typically, the bracket is adjustable so as to direct at least two of the radiation sources to irradiate a common region of the skin, and so as to direct the at least two of the radiation sources to irradiate different regions of

5 the skin.

Additionally or alternatively, the plurality of radiation sources includes an array of solid-state radiation sources, including first radiation sources, which emit the radiation in the first wavelength band, and second radiation sources, which emit the

10 radiation in the second wavelength band. Typically, the solid-state radiation sources are selected from a group of sources consisting of light-emitting diodes (LEDs) and laser diodes. In a disclosed embodiment, the first radiation sources include at least one of GaAs and GaAlAs diodes, while the second radiation sources includes at least one of GaN, SiN, InSiN, and SiC diodes.

15

Typically, the at least one radiation source includes a spectral filter, for blocking ultraviolet (UV) radiation generated by the at least one radiation source. Additionally or alternatively, the at least one radiation source includes a forced air cooling device for cooling the skin that is irradiated by the at least one radiation

20 source. Further additionally or alternatively, the at least one radiation source is adapted to be placed in contact with the skin.

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There is additionally provided, in accordance with an embodiment of the present invention, a lamp, including:

an envelope, which is at least partly transparent;

an excitation circuit, which is coupled to the lamp so as excite an electrical  
5 discharge within the envelope; and

a gas and metal mixture, contained within the envelope, which is adapted, upon excitation of the electrical discharge by the excitation circuit, to emit both narrowband infrared (IR) radiation in a first wavelength band and narrowband violet/blue light in a second wavelength band.

10

Typically, the first wavelength band is in the range 800-980 nm, and the second wavelength band is in the range 405-450 nm. In a disclosed embodiment, the first wavelength band is in the range 850-910 nm.

15 In some embodiments, the gas mixture includes metal halide materials selected to radiate in the first and second wavelength bands. Typically, the metal halide materials include gallium and cesium halides. Additionally or alternatively, the gas mixture further includes mercury. Further additionally or alternatively the excitation circuit includes electrodes, which are spaced a predetermined distance  
20 apart within the envelope.

The present invention will be more fully understood from the following detailed description of the embodiments thereof, taken together with the drawings in which:

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic, pictorial illustration of a system for phototherapy, in accordance with an embodiment of the present invention;

5

Figure 2 is a schematic, sectional view of a radiator for use in phototherapy, in accordance with an embodiment of the present invention;

Figure 3 is a schematic side view of a discharge lamp, in accordance with an embodiment of the present invention;

10

Figure 4 is a schematic spectral diagram showing an emission spectrum of a discharge lamp, in accordance with an embodiment of the present invention;

Figure 5 is a schematic, pictorial illustration of a system for phototherapy, in accordance with an alternative embodiment of the present invention; and

15

Figure 6 is a schematic front view of a radiator for use in phototherapy, in accordance with an alternative embodiment of the present invention.

20

Figure 7 is a schematic presentation of a commercial unit which utilize the current invention and separately treats each side of the face.

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Figure 8 is a schematic presentation of a commercial unit which utilize the current invention and simultaneously treats both sides of the face.

### DETAILED DESCRIPTION OF EMBODIMENTS

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Figure 1 is a schematic, pictorial illustration of a system 20 for phototherapy, in accordance with an embodiment of the present invention. System 20 is used to treat inflammations of the skin, such as an ulcer on a leg 22 of a patient. The system in this embodiment comprises two radiators 24 and 26, each comprising a  
10 lamp 23, a lamp holder 25, a reflector 27 and an optical filter 29, which are described in greater detail herein below. Each radiator may be enclosed in a metal or a plastic housing, not shown here. Typically, both of radiators 24 and 26 emit both violet/blue and IR radiation. Alternatively, one of the radiators may emit violet/blue radiation, while the other emits IR radiation. Further alternatively, system  
15 20 may comprise only a single radiator (emitting both violet/blue and IR) or three or more radiators.

Radiators 24 and 26 are mounted on an adjustable bracket 28, which allows the positions and angular orientations of the radiators to be adjusted. Thus, bracket  
20 28 may be set so that both radiators are aimed toward the same region of the patient's skin, as shown in Figure 1. Alternatively, bracket 28 may be adjusted so that each radiator irradiates a different region, so that a large area of the skin can be treated at one time. Bracket 28 and radiators 24 and 26 are coupled to a control



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and power supply console unit 30 by an adjustable arm 32 and a joint module 34. The arm and joint module together permit flexible 3D positioning of the radiators, so as to enable treatment of all body parts of both seated and reclining patients. The console 30 comprises a power supply module for operating the radiators and user  
5 controls 31 for setting treatment parameters, such as the treatment duration and power level of irradiation.

Typically, radiators 24 and 26 emit violet/blue light in the range of 405-450 nm, for anti-inflammatory effect, and IR radiation in the range of 800-980 nm for  
10 vascular dilation. Preferably, radiators 24 and 26 are narrowband sources, meaning that most of the radiation emitted by the radiators falls within bands no more than 100 nm wide in the violet/blue and IR spectral ranges. Most preferably, most of the IR radiation is emitted in a band between 850 and 910 nm. Absorption of radiation in this wavelength range by hemoglobin in the blood is believed to cause the  
15 hemoglobin to release NO (nitric oxide), which is then absorbed in the blood vessel walls, causing them to dilate. The lifetime of NO in the blood is approximately 10 sec. Therefore, the effect of the IR irradiation by radiators 24 and 26 is local and temporary. To take advantage of this effect, the radiators may either emit the violet/blue and IR radiation simultaneously, or they may emit the IR and violet/blue  
20 radiation in sufficiently rapid succession so that the violet/blue radiation is applied while the blood vessels are dilated.

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For effective treatment of skin inflammation, the violet/blue light intensity on the patient's skin should typically be at least  $4 \text{ mW/cm}^2$ , while the IR intensity is at least  $1 \text{ mW/cm}^2$ . For more rapid treatment, the violet/blue light intensity may be  $20 \text{ mW/cm}^2$  or greater, while the IR intensity is  $9 \text{ mW/cm}^2$  or greater. Typically, the radiators are set to operate continuously for periods of one minute or more. Alternatively, the radiators may operate in pulsed modes, with accumulated pulse intensities of at least  $200 \text{ mJ/cm}^2$  in the violet/blue range and  $60 \text{ mJ/cm}^2$  in the IR. The treatment area is determined by the area of the inflammation, and typically varies between about  $5 \times 5$  and  $30 \times 30 \text{ cm}$ . The total radiation dosage depends on the type of condition and its extent. For healing skin ulcers, for example, a regimen of daily treatments of 30 minutes each over a period of two to three weeks, with a dose per treatment of  $30 \text{ J/cm}^2$ , is believed to be effective.

Figure 2 is a schematic, sectional illustration showing details of radiator 24, in accordance with an embodiment of the present invention. (The same design may be used for radiator 26.) The radiator comprises a lamp 40, typically a gas discharge lamp, which emits both violet/blue and IR radiation, as described further hereinbelow. A reflector 42 collects and reflects the radiated energy from the lamp 40 toward the patient's skin. The reflector may have a parabolic cross-section, for example, or it may be specially designed with multiple curved reflective facets. A filter 44 blocks ultraviolet (UV) radiation output below about  $400 \text{ nm}$ . Filter 44 may comprise, for example, a GG400 UV-blocking filter, approximately 4 to 6 mm thick, produced by Schott Optics Division (Mainz, Germany). One or more fans 46 or

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other types of ventilators or blowers may be mounted on radiator 24 in order to cool the treated area of the skin.

Figure 3 is a schematic side view of lamp 40, in accordance with an embodiment of the present invention. The lamp comprises a transparent quartz tube 50, about 8-14 mm in diameter, containing at least two electrodes 52 separated by a gap of about 30 to 40 mm. The electrodes are coupled to terminals 54 so as to define an excitation circuit, which is connected to the power supply that drives the lamp. Typically, the excitation circuit is driven by an electrical current between 3.0 and 3.6 A, at 115 VAC. Alternatively, both higher- and lower-power AC and DC voltage-driven lamps and other types of discharge excitation circuits, as are known in the art, may be used in system 20.

Lamp 40 is filled with a novel combination of gases and metals in order to provide simultaneous violet/blue and IR narrowband emission. Tube 50 is first evacuated to a high vacuum in order to eliminate all atmospheric gases and humidity. The tube is then filled with about 40 mg of pure mercury, about 0.2 mg of a gallium halide, and about 0.1 to 0.5 mg of a cesium halide. The gallium and cesium halides typically comprise bromides or iodides or a combination of the two. The gallium halide causes the lamp to emit strongly on lines in the 405-450 nm range, while the cesium halide causes IR emission on lines in the 850-910 nm range. Depending on the amount of cesium halide in the tube, the IR emission accounts for between 10% and 50% of the total optical power output of the lamp.

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Figure 4 is a schematic typical spectral diagram showing an output spectrum 70 of lamp 40, in accordance with an embodiment of the present invention. Strong violet/blue lines 72 are seen in the 405-450 nm range due to the gallium in the lamp, along with IR lines 74 at 852 nm and 894 nm due to the cesium. The two blue and near infrared bands are schematically marked by the two curves "BLUE" and "NEAR INFRARED". A lamp produced to the above specifications by Lamptech Ltd. (Ashkelon, Israel) gave optical power density on the skin, when installed in system 20, over  $30 \text{ mW/cm}^2$  in the violet/blue and IR bands together.

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Figure 5 is a schematic, pictorial illustration of a system 80 for phototherapy, in accordance with another embodiment of the present invention. System 80 in this embodiment shown in another treatment application-treating skin inflammation on a face 82 of a patient-but is otherwise functionally similar to system 20. Radiators 84 and 86 in this case comprise panels with multiple miniature solid-state emitters, such as light-emitting diodes (LEDs), mounted on the panels. The emitters may be organized in a single-dimensional or a two-dimensional diode matrix array. As in system 20, both of radiators 84 and 86 typically emit radiation in both the violet/blue and near IR bands. Alternatively, one of the radiators may emit violet/blue radiation, while the other emits IR, either simultaneously or in succession. Greater or smaller numbers of radiators may be used. As a further alternative, one of the radiators may comprise an array of miniature emitters, and the other may comprise a gas

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discharge lamp, as described above, or a single radiator may comprise both a matrix of miniature emitters and a gas discharge lamp.

Figure 6 is a schematic front view of radiator 84, in accordance with an embodiment of the present invention. In this embodiment, the radiator comprises a panel 90, preferably curved, on which a two-dimensional matrix array of high-intensity solid-state radiation sources 92 and 94 are mounted. Typically, sources 92 comprise, GaN, SiN, InSiN or SiC (silicon carbide) based LEDs, or other diode lasers or LEDs of other types that emit violet/blue light. Sources 94 comprise IR-emitting LEDs, such as GaAlAs diodes or GaAs diodes, or laser diodes. The power density requirements of radiator 84 are similar to those of radiator 24, as described above. Suitable violet/blue LEDs are produced, for example, by Nichia Chemical Industries Ltd. (Tokyo, Japan), LumiLED (San Jose, California) and HP/Agilent (PALO ALTO, California). High-intensity IR LEDs are made by many manufacturers, such as LumiLED, Kingbright (Taipei Hsien, Taiwan) and Fairchild Semiconductor (Irvine, Texas). The LEDs in radiator 84 may be wired and controlled separately or in matrix groups.

Although in the embodiment shown in Figure 5, radiators 84 and 86 are spaced away from the skin, in other embodiments panel 90 may have the form of a mask, which contacts the skin. The mask might also include thermoelectric cooler elements (TEC) to cool the irradiated skin. The mask may be placed against the skin in combination with a suitable cream or other medication, such as glycolic acid or

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other antioxidants or peeling creams. Alternatively, the mask may be used without cream or medication. Systems 20 and 80 (and other implementations of the present invention) may be used in treating a wide range of inflammatory skin conditions, including:

- 5     • Ulcers (as detailed above).
- Skin aging, particular in heavy smokers, who tend to have yellowish skin due to reduced blood flow to the skin. These patients' skin suffers from both insufficient capillary supply and chronic subclinical inflammation, both related to the effects of smoking. Chronic exposure to heavily polluted air or  
10    excessive sunlight may have similar effects. The skin in these cases may be treated by violet/blue and IR radiation, possibly in combination with fruit acids, such as glycolic acid, and other creams. A course of five to fifteen treatments is expected to visibly improve the skin condition, and can be followed subsequently by periodic maintenance treatments.
- 15    • Post-surgical edema and redness of the skin. Liposuction, for example, may be followed by marked edema and changes of skin color, which may be relieved by a small number of treatments with violet/blue and IR radiation at high intensity (over 20 mW/cm<sup>2</sup> violet/blue and 8 mW/cm<sup>2</sup> IR radiation).
- Rosacea, grades II and III.
- 20    • Chronic cutaneous inflammatory conditions, such as atopic dermatitis.
- Acne-related inflammations.

Other applications of violet/blue and IR radiation in reducing inflammation will be apparent to those skilled in the art.

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Figure 7 presents an embodiment of the current invention which has been commercialized and treats each side of the face separately. The treatment head 700 incorporates a light source and a treatment window 701 which filters UV light and transmits both blue and near infrared light. The treatment head is adjustable and can be aimed at the patient head in sitting or laying position. A removable filter 702 (not drawn) can be added or removed with two screws. The filter transmits blue light and blocks infrared light. The filter is utilized when acne problems are being treated and pure blue light is recommended. The filter is removed when near infrared light and blue light are recommended. The treatment head is attached to a mast 703, the height of which is electrically controlled. An electrical control panel 704 enables the setting of the treatment duration, as well as the turning ON and OFF of an air fan which helps chilling the face.

Figure 8 presents a system which treats both sides of the face simultaneously. The system incorporates a light head 800 which incorporates two lamps located on both sides of the head. Filters 806 (only one of them is shown in the figure) rejects any UV light and transmits blue and near infrared light. By adding a filter 807 (not shown) which rejects near infrared light to the filter 806, it is possible to provide treatments which require only blue light. The treatment head is attached to a mast 804, the height of which is electrically controlled. A panel 810 enables the control of the treatment duration, the mast height and also serves as a computerized data base which can be fed by patients condition and patient picture. Fans and a

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camera are located in zone 801. The unit is transportable from room to room and incorporates wheels 820.

Example 1 :

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The system has been utilized for the treatment of aging skin in a clinic in Montpellier (France) and a clinic in Tel Aviv (Israel). Over 15 patients have been treated from a distance of 20 cm at a power level of 20 milliwatts / cm<sup>2</sup> in both 405-420 nm and 850-890 nm band widths. The number of treatments was 6-8 and combined with

10 Glycolic acid. Results showed clear reduction of pores, pigmentation and improvement of skin color.

Example 2:

15 A system was utilized in a clinic for the reduction of the erythema duration after laser skin resurfacing. Normally, post skin resurfacing average erythema duration is 3 weeks. Patients have been treated for 5 days starting one day after skin resurfacing. Erythema faded much faster than without the utilization of the blue/infrared source and lasted only 10 days.

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Example 3:

A system which combines blue and near infrared light was utilized to treat patients immediately after face lifting surgery. A patient was treated with light for 6 days after surgery on one side of the face. The other side was not treated. The treated side doesn't show any redness on the suture line, whereas redness can be seen on the control untreated site. The three examples demonstrate the healing effect of the combination of blue and near infrared light, as utilized by a commercial unit based on the current invention.

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Although the embodiments described above are based on certain particular treatment systems and types of radiation sources, the principles of the present invention may similarly be applied in other system configurations and using other suitable radiation sources, as will be apparent to those skilled in the art.

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It will thus be appreciated that the embodiments described above are cited by way of example, and that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof which would occur to persons skilled in the art upon reading the foregoing description and which are not disclosed in the prior art.

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WHAT IS CLAIMED IS:

1. A method for treating skin conditions with associated inflammation in skin of a patient, comprising irradiating the skin with substantially narrow band  
5 infrared (IR) radiation in a first wavelength band and with substantially narrow band violet/blue light in a second wavelength band.

2. The method according to claim 1, wherein the first wavelength band is selected to cause dilation of blood vessels in a vicinity of the inflammation, and  
10 wherein irradiating the skin with the violet/blue light comprises applying the violet/blue light to the inflammation while the blood vessels are dilated.

3. The method according to claim 2, wherein irradiating the skin comprises irradiating the skin with the IR radiation and the violet/blue light  
15 simultaneously.

4. The method according to claim 2, wherein irradiating the skin comprises irradiating the skin with the IR radiation and the violet/blue light sequentially.

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5. The method according to claim 1, wherein the first wavelength band is in the range 800-980 nm, and the second wavelength band is in the range 405-450 nm.

5 6. The method according to claim 5, wherein the first wavelength band is in the range 850-900 nm.

7. The method according to claim 1, wherein irradiating the skin comprises irradiating the skin with at least 4 mW/cm<sup>2</sup> of the violet/blue light and at  
10 least 1 mW/cm<sup>2</sup> of the IR radiation.

8. The method according to claim 7, wherein irradiating the skin comprises irradiating the skin with at least 20 mW/cm<sup>2</sup> of the violet/blue light and at  
least 8 mW/cm<sup>2</sup> of the IR radiation.

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9. The method according to claim 1, wherein irradiating the skin comprises irradiating the skin continuously for at least one minute.

10. The method according to claim 1, wherein irradiating the skin  
20 comprises irradiating the skin with pulsed radiation.

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11. The method according to claim 1, wherein irradiating the skin comprises irradiating the skin using a single radiation source, which emits both the substantially narrow band violet/blue light and the substantially narrow band IR radiation.

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12. The method according to claim 11, wherein the single radiation source comprises a discharge lamp containing metal halide materials selected to radiate in the first and second wavelength bands.

10 13. The method according to claim 1, wherein irradiating the skin comprises irradiating the skin using an array of solid-state radiation sources.

14. The method according to claim 1, wherein the skin conditions are selected from the group consisting of skin aging, ulcers, edema, rosacea, chronic  
15 cutaneous inflammatory conditions and acne, post surgical healing and reduction of erythema duration in post skin resurfacing.

15. The method according to claim 14, and comprising applying a medicated cream to the skin in conjunction with irradiating the skin.

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16. The method according to claim 1, wherein irradiating the skin comprises irradiating the skin using a radiation source that is in contact with the skin.

17. Apparatus for treating skin conditions and associated inflammation in skin of a patient, comprising at least one radiation source, which is adapted to irradiate the skin with substantially narrow band infrared (IR) radiation in a first wavelength band and with substantially narrow band violet/blue light in a second wavelength band.

18. The apparatus according to claim 17, wherein the first wavelength band is selected to cause dilation of blood vessels in a vicinity of the inflammation, and wherein irradiating the skin with the violet/blue light comprises applying the violet/blue light to the inflammation while the blood vessels are dilated.

19. The apparatus according to claim 18, wherein the at least one radiation source is adapted to irradiate the skin with the IR radiation and the violet/blue light simultaneously.

20. The apparatus according to claim 18, wherein the at least one radiation source is adapted to irradiate the skin comprises irradiating the skin with the IR radiation and the violet/blue light sequentially.

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21. The apparatus according to claim 17, wherein the first wavelength band is in the range 800-980 nm, and the second wavelength band is in the range 405-450 nm.

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22. The apparatus according to claim 21, wherein the first wavelength band is in the range 850-910 nm.

23. The apparatus according to claim 17, wherein the at least one radiation  
10 source is adapted to irradiate the skin with at least 4 mW/cm<sup>2</sup> of the violet/blue light and at least 1 mW/cm<sup>2</sup> of the IR radiation.

24. The apparatus according to claim 23, wherein the at least one radiation  
source is adapted to irradiate the skin with at least 20 mW/cm<sup>2</sup> of the violet/blue light  
15 and at least 9 mW/cm<sup>2</sup> of the IR radiation.

25. The apparatus according to claim 17, wherein the at least one radiation source is adapted to irradiate the skin continuously for at least one minute.

20 26. The apparatus according to claim 17, wherein the at least one radiation source is adapted to irradiate the skin with pulsed radiation.

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27. The apparatus according to claim 17, wherein the at least one radiation source comprises a single radiation source, which emits both the violet/blue light and the IR radiation.

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28. The apparatus according to claim 27, wherein the single radiation source comprises a discharge lamp containing metal halide materials selected to radiate in the first and second wavelength bands.

10 29. The apparatus according to claim 28, wherein the metal halide materials comprise gallium and cesium halides.

30. The apparatus according to claim 17, wherein the at least one radiation source comprises a plurality of radiation sources.

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31. The apparatus according to claim 30, further comprising an adjustable bracket, on which the radiation sources are mounted, so as to allow a relative angular orientation of the radiation sources to be adjusted.

20 32. The apparatus according to claim 31, wherein the bracket is adjustable so as to direct at least two of the radiation sources to irradiate a common region of

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the skin, and so as to direct the at least two of the radiation sources to irradiate different regions of the skin.

33. The apparatus according to claim 30, wherein the plurality of radiation  
5 sources comprises an array of solid-state radiation sources, comprising first  
radiation sources, which emit the radiation in the first wavelength band, and second  
radiation sources, which emit the radiation in the second wavelength band.

34. The apparatus according to claim 33, wherein the solid-state radiation  
10 sources are selected from a group of sources consisting of light-emitting diodes  
(LEDs) and laser diodes.

35. The apparatus according to claim 34, wherein the first radiation  
sources comprise at least one of GaAs and GaAlAs diodes, while the second  
15 radiation sources comprises at least one of GaN, SiN, InSiN, and SiC diodes.

36. The apparatus according to claim 17, wherein the at least one radiation  
source comprises a spectral filter, for blocking ultraviolet (UV) radiation generated by  
the at least one radiation source.

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37. The apparatus according to claim 17, wherein the at least one radiation source comprises a forced air cooling device for cooling the skin that is irradiated by the at least one radiation source.

5 38. The apparatus according to claim 17, wherein the at least one radiation source is adapted to be placed in contact with the skin.

39. A lamp, comprising:  
an envelope, which is at least partly transparent;  
10 an excitation circuit, which is coupled to the lamp so as excite an electrical discharge within the envelope; and  
a gas and metal mixture, contained within the envelope, which is adapted, upon excitation of the electrical discharge by the excitation circuit, to simultaneously emit radiation in both narrowband 405-420 nm and narrow band 850-890 nm  
15 radiation, said gas and metal mixture comprises of mercury, gallium halide and cesium halides.

40. The lamp according to claim 39, wherein the excitation circuit comprises electrodes, which are spaced a predetermined distance apart within the  
20 envelope.

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41. The apparatus according to claim 17

(a) a self supporting mechanical fixture for holding the at least one radiation source in a fixed position spaced apart from the skin during treatment thereof, said mechanical fixture comprising securing means for operatively  
5 securing the at least one radiation source to the fixture and adjustment means for adjusting the distance or position of the at least one radiation source from the treatment area, said securing means of the mechanical fixture securing the at least one radiation source in said fixed position when the radiation source is emitting the radiation and/or light;

10 (b) an optical system for collecting and shaping the infrared radiation and the violet/blue light in advance of delivering the infrared radiation and the violet/blue light to the skin; and

(c) electronic means for controlling parameters associated with the infrared radiation and the violet/blue light.

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42. The method according to claim 1 comprising:

(a) positioning in an operative treating position for treating the skin condition and associated inflammation, a self supporting mechanical fixture comprising at least one radiation source in a fixed position spaced apart from the  
20 skin, said mechanical fixture comprising securing means for operatively securing the radiation source to the fixture, and adjustment means for adjusting the distance or position of the radiation source from the skin; and

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(b) applying to the skin said substantially narrow band infrared radiation and said substantially narrow band violet/blue light.

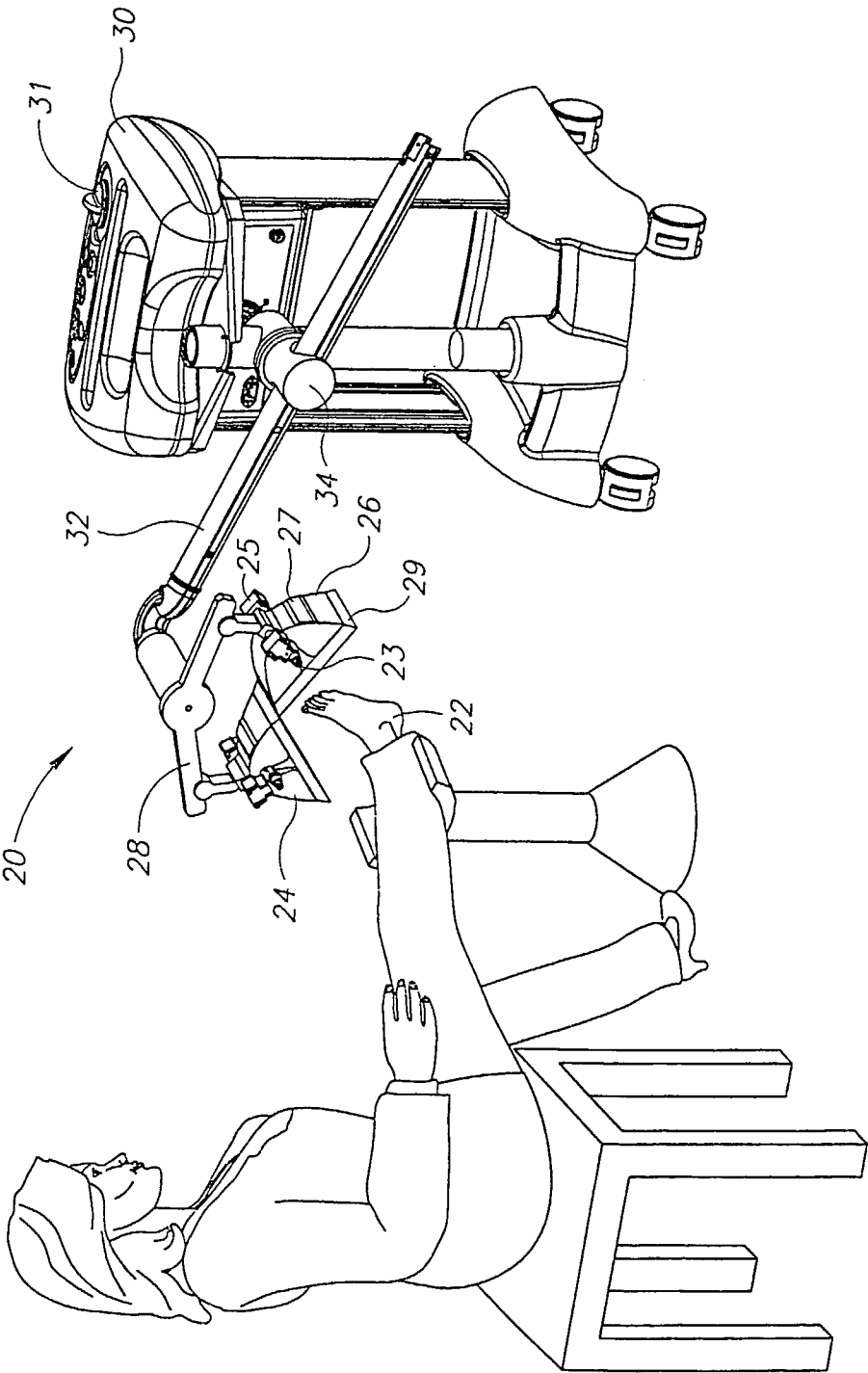


FIG.1

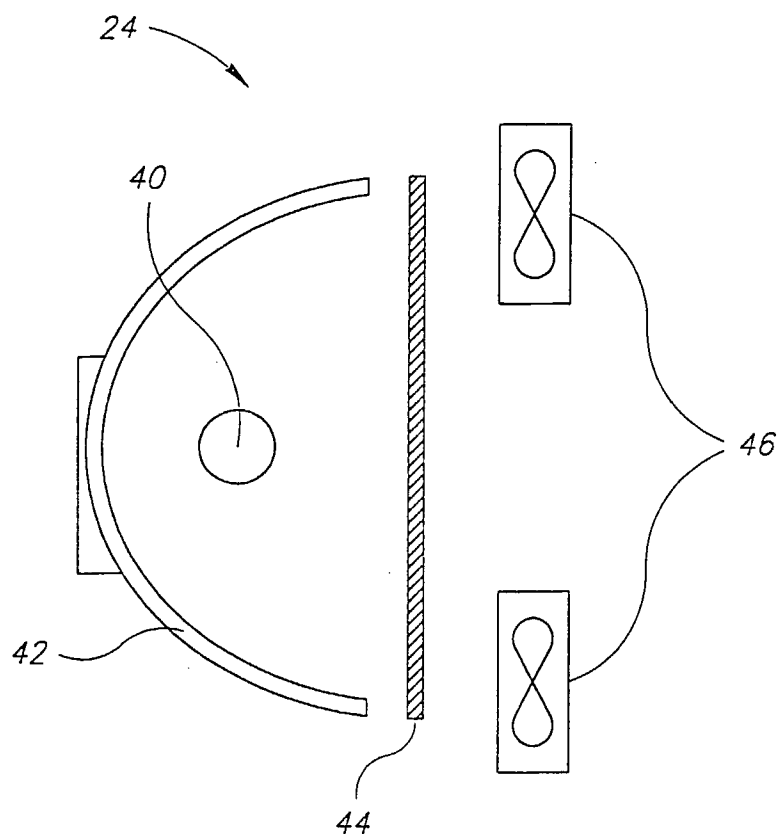


FIG. 2

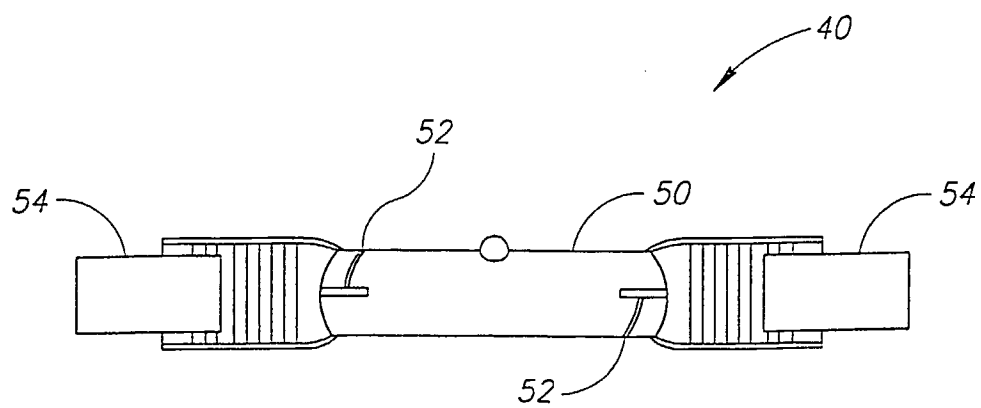


FIG. 3

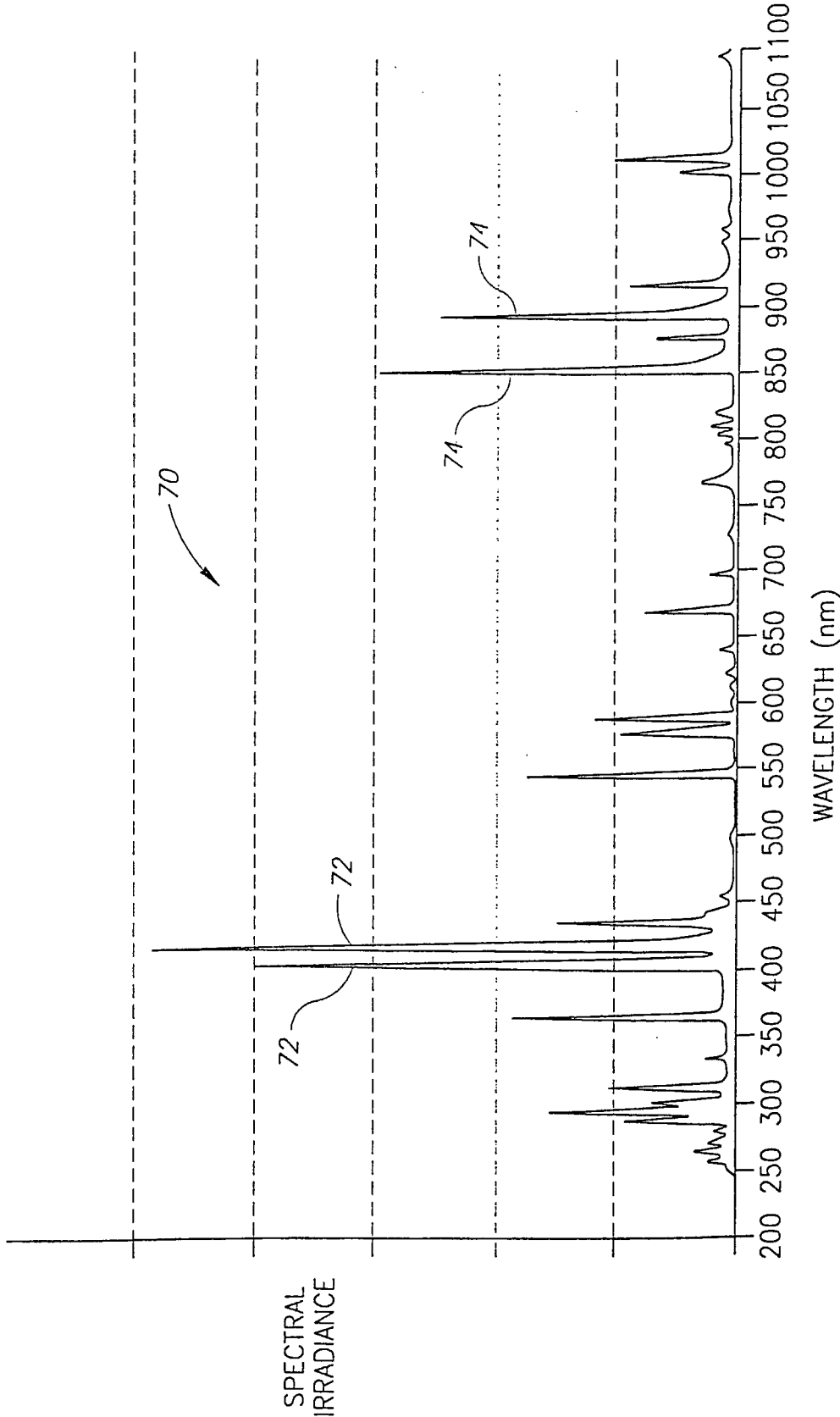


FIG.4

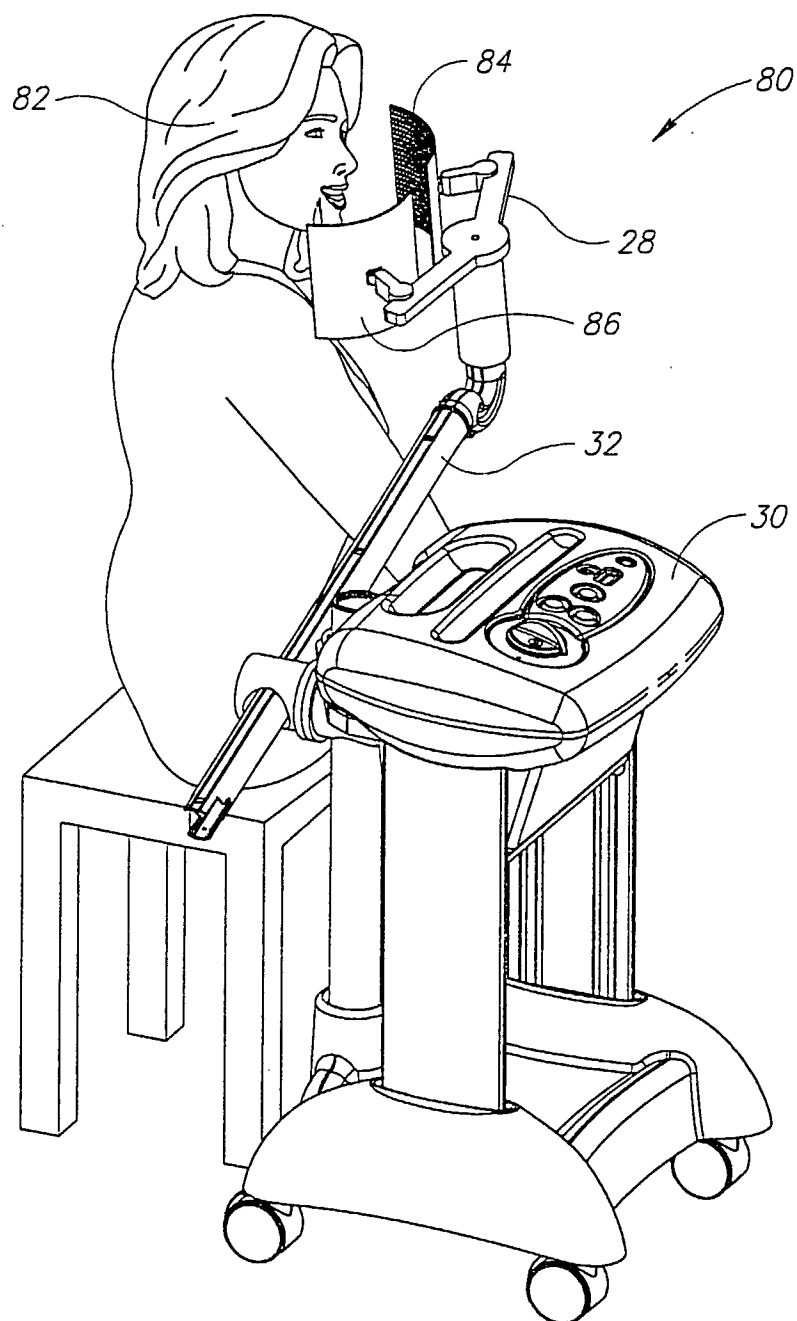


FIG.5

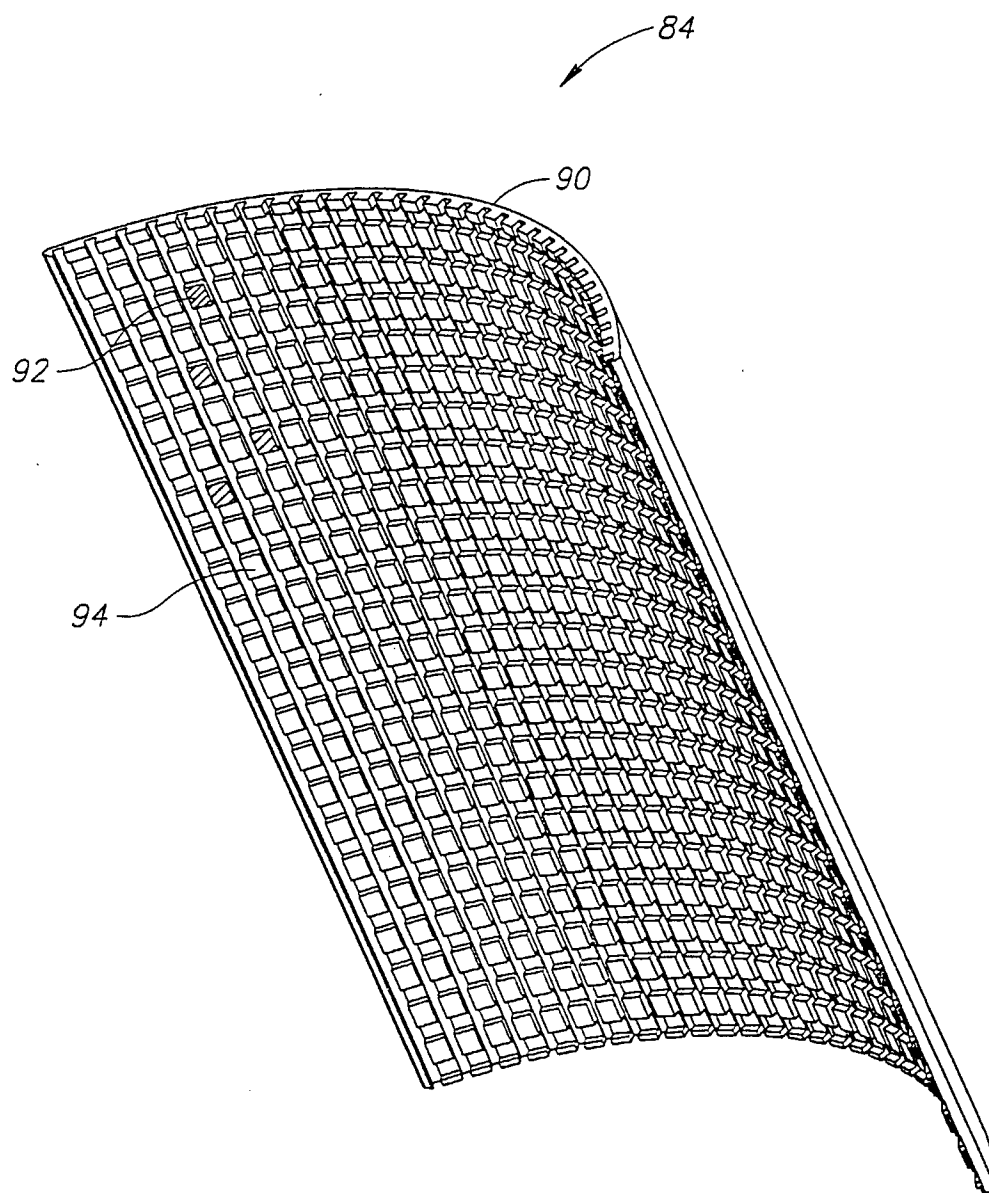


FIG. 6



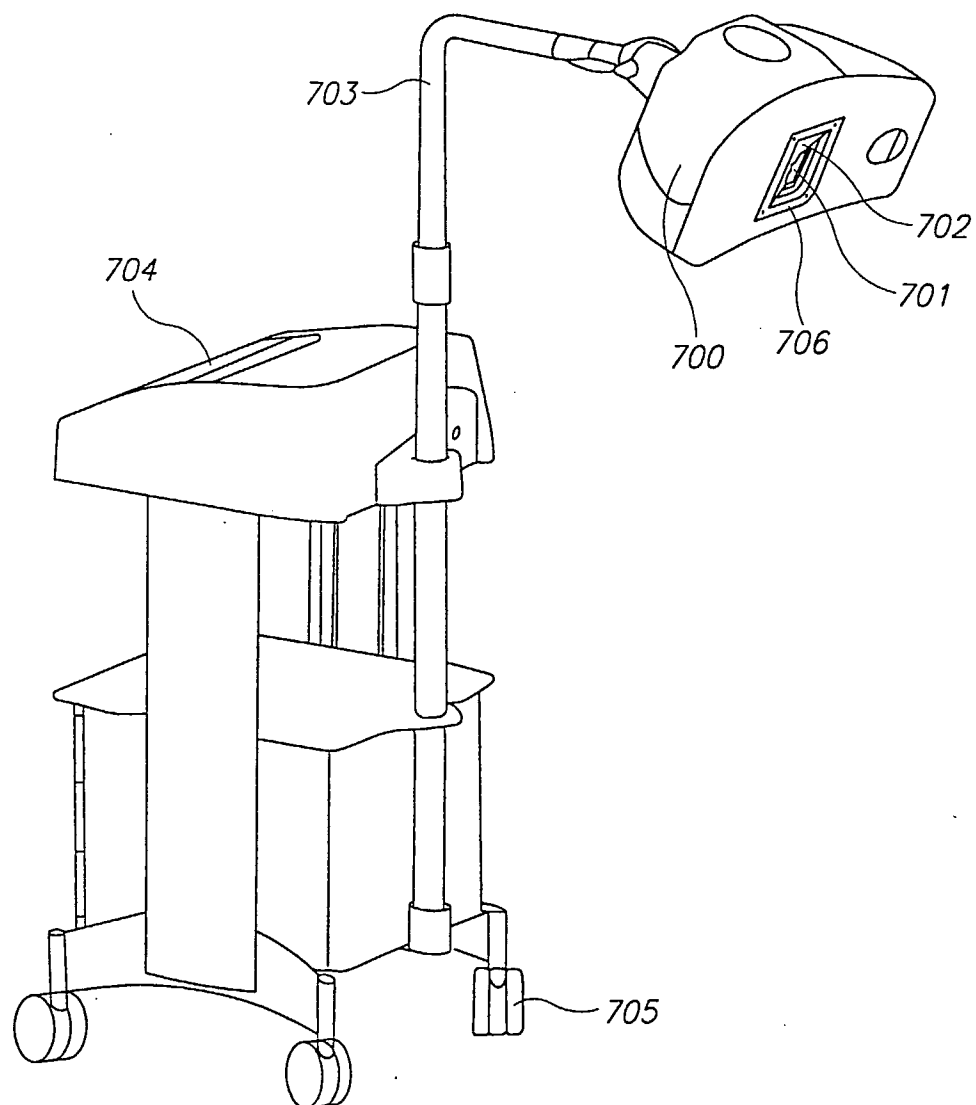


FIG. 7

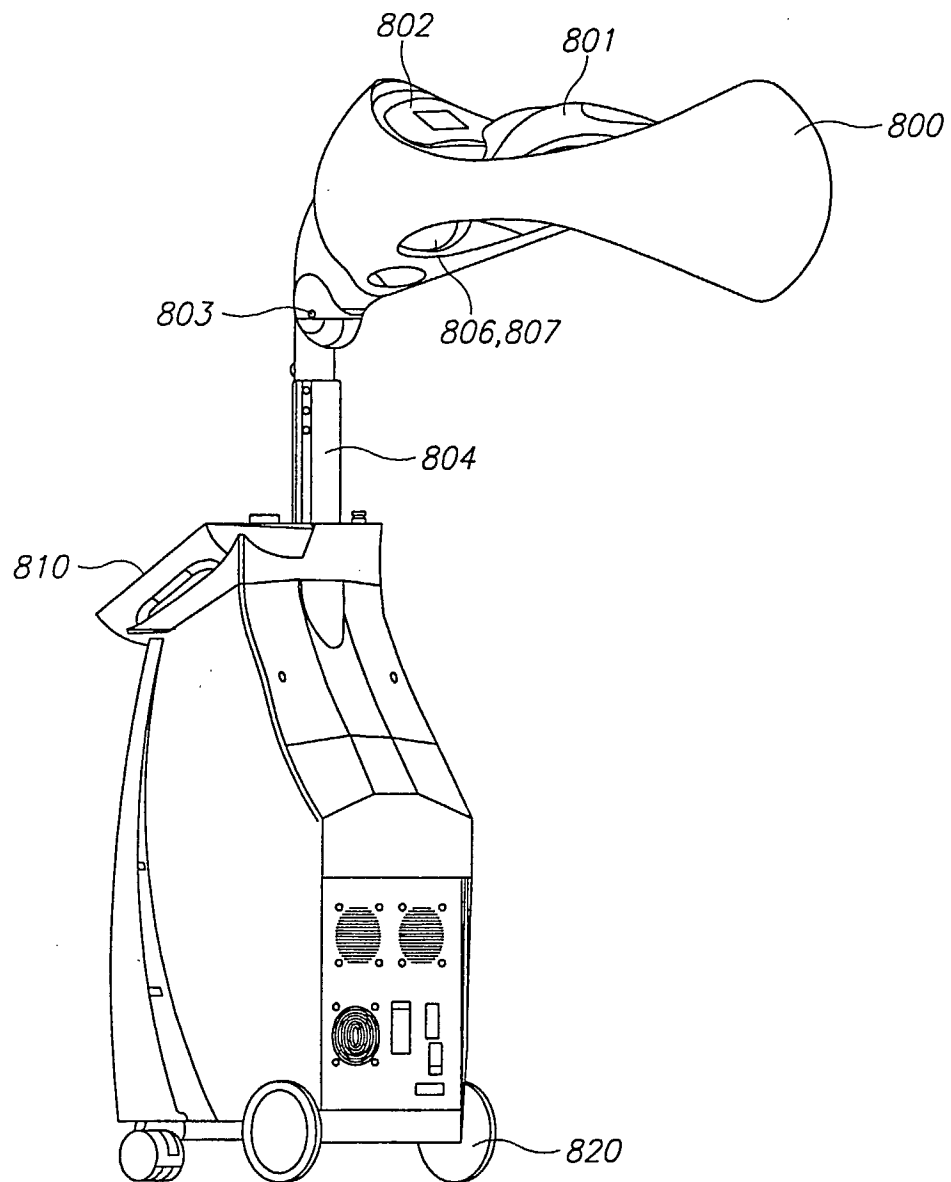


FIG. 8

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(54) Title: MULTI-SPOT LASER SURGICAL APPARATUS AND METHOD

(57) Abstract: An array of light beams is swept along a main scan direction and dithered in a sub-scan direction to generate a treatment pattern of spots. The array is elongated along the sub-scan direction and the dithering has a travel that is significantly less than the length of the array in the sub-scan direction.



WO 2005/065288 A2

**MULTI-SPOT LASER SURGICAL APPARATUS AND METHOD**

Inventors: Robert Kehl Sink

**BACKGROUND OF THE INVENTION**1. **Field of the Invention**

[0001] This invention relates generally to an array of light beams used to generate a pattern of spots, for example as can be employed in laser surgery and laser dermatology.

2. **Description of the Related Art**

[0002] In laser surgical applications, for example in laser dermatology, an optical system generates a light beam(s) of a desired size and energy and this light beam is used to treat a selected region of the patient's body (i.e., the treatment area). For example, in many dermatology applications, a hand piece is used to guide the laser beam to the treatment area. The hand piece is typically attached to one end of an articulated arm, which transmits the laser beam to the hand piece and also supports a wide range of motion for the hand piece.

[0003] A physician typically treats the treatment area by sweeping the laser hand piece back and forth over the treatment area. In many cases, the physician is guided by an aiming line, which may be generated by the hand piece. The sweeping may be either manual or automated. Automated sweeping can be achieved by mounting the laser or other light source on a movable carriage. Whatever the mechanism, as the laser beam is swept over the treatment area, the physician typically pulses the laser beam on and off, either manually or via automatic means, thereby regulating the exposure of the treatment area and creating a pattern of treatment spots over the treatment area.

[0004] Many laser technologies for dermatology use a single high power beam that is scanned across the treatment area to create a pattern of exposed areas or spots. In many cases, the spots overlap sufficiently that the entire treatment area is exposed. The treatment rates achievable by scanning a single beam in this manner can be sufficiently fast when a high power laser (typically >10 W) is used with a large diameter beam (typically 2-6 mm).

[0005] However, new treatments can use smaller spot sizes and more spots. For example, see co-pending U.S. Patent Applications Ser. No. 10/367,582, "Method and Apparatus for Treating Skin Using Patterns of Optical Energy," filed on February 14, 2003; and Ser. No. 60/486,304, "Method and Apparatus for Fractional Phototherapy of Skin," filed 5 July 11, 2003; both of which are incorporated herein by reference. Traditional laser systems are not well suited for these applications because the laser beams generated by traditional systems typically are too large and too energetic. Traditional systems also are typically based on more expensive types of lasers and do not take advantage of lower power, cheaper semiconductor lasers. In addition, the single laser beam generated by traditional systems 10 would have to be individually positioned to generate each of the spots in the overall pattern and, since there typically are a large number of spots in the pattern, the required scan time becomes unacceptably long.

[0006] Hence, there is a need for devices and methods that can generate a pattern of spots on a treatment area, preferably in an efficient manner.

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### SUMMARY OF THE INVENTION

[0007] The present invention overcomes the limitations of the prior art by providing a laser treatment apparatus in which an array of light beams is used to generate a treatment pattern of spots. In one approach, the array is swept along a main scan direction and dithered 20 in a sub-scan direction to generate the pattern of spots. The array is elongated along the sub-scan direction and the dithering has a travel that is significantly less than the length of the array in the sub-scan direction.

[0008] The optical module that generates the array of light beams can take many different forms. For example, it can be based on a fiber coupled laser source diode, a laser 25 source followed by beam splitting optics, a fiber laser source followed by a beam splitter, multiple light sources each of which generates one of the light beams in the array, or an external light source(s) for example coupled by an optical fiber. The light beams in the array can also be generated simultaneously, sequentially (e.g., by scanning a single light beam to multiple locations), or a combination of the two. The sub-scan module that dithers the array of

light beams can also take many different forms. A movable carriage that can be translated in the sub-scan direction and a light deflecting module are two examples.

[0009] In one embodiment, multiple laser diodes are coupled into optical fibers. The terminating ends of the optical fibers are aligned into a 1xN array and imaged onto the treatment area to generate the spots. The total length of the array is approximately 1 cm. The array is dithered to form an irregular pattern of spots (e.g., see FIG. 3). The travel for the dithering is approximately equal to the spacing between light beams in the array. The dithering is accomplished by components in a hand piece; the hand piece is swept along the main scan direction. A main scan sensor tracks the velocity of the sweeping and a controller adjusts the dithering accordingly. The controller also controls the exposure of the light beams on the treatment area so that the spots are not over- or underexposed.

[0010] Other aspects of the invention include methods and systems corresponding to the apparatus described above, and applications for the above. One example application is medical treatments that use smaller spot sizes (for example, spots with diameters of 0.1 mm) and more spots (for example, spot densities of 2000 spots/cm<sup>2</sup>) than conventional laser treatments. For example, see co-pending U.S. Patent Applications Ser. No. 10/367,582, "Method and Apparatus for Treating Skin Using Patterns of Optical Energy," filed on February 14, 2003; and Ser. No. 60/486,304, "Method and Apparatus for Fractional Phototherapy of Skin," filed July 11, 2003.

#### BRIEF DESCRIPTION OF THE DRAWINGS

[0011] These and other objects, features and advantages can be more readily understood from the following detailed description with reference to the accompanying drawings, wherein:

[0012] FIG. 1 is a diagram showing a pattern of spots generated by an array of light beams using a raster scan.

[0013] FIG. 2 is a diagram showing a pattern of spots generated by an array of light beams according to the invention.

[0014] FIG. 3 is a diagram showing another pattern of spots generated by an array of light beams according to the invention.

[0015] FIG. 4 is a block diagram of a light treatment apparatus for generating an array of light beams according to the invention.

[0016] FIG. 5 is a diagram of one implementation of a light treatment apparatus using a single light source.

5 [0017] FIG. 6 is a diagram of another implementation of a light treatment apparatus using multiple light sources.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0018] FIG. 1 shows a raster pattern for generating a pattern of spots. The row 150 of  
10 laser beams is aligned to the main scan direction 110 (i.e., the direction in which the physician sweeps the hand piece). While the array 150 is swept along the main scan direction 110, it is also raster scanned in the transverse direction 120. The laser beams are pulsed during this movement to produce the pattern of spots shown in FIG. 1. At the end 132 of each raster scan, the array is "reset" to the start position 134 of the next raster scan.

15 [0019] While this approach has many advantages compared to individually positioning a single laser beam to generate each of the spots in the pattern, one disadvantage of this approach is the travel 190 of the array 150 in the raster scan direction 120 can be long in certain applications. If the raster scan is accomplished by mechanically translating the light source, then the long travel increases the mechanical wear and tear and reduces the life of the  
20 system. The long travel can also make the hand piece bulky and reduce the speed or resolution of the overall scan. The raster scan pattern also leaves a tapered gap 170 at the start and end of the overall pattern. This type of raster scan also creates a regular pattern of spots. Artifacts of the regular pattern can be visible even when the individual spots are not, and this can be cosmetically undesirable.

25 [0020] FIG. 2 shows another approach for generating a treatment pattern. In this example, a 1x5 array 250 of light beams is aligned to be transverse to the main scan direction 210. As the array 250 is swept along the main scan direction 210, it is also dithered in the transverse sub-scan direction 220. In FIG. 2, the array is dithered to four different offsets in the sub-scan direction, beginning with 231 and ending with 234. It is then reset to the start

position 235 for the next set of sub-scans. The total travel 290 in the sub-scan direction is significantly less than the length of the array in the sub-scan direction. In this example, the light beams (and resulting spots) are evenly spaced and the travel 290 in the sub-scan direction is approximately equal to the beam-to-beam spacing.

5 [0021] FIG. 3 shows another treatment pattern generated according to the invention. This example uses a 1x7 array 350 of light beams. The array 350 is dithered in the sub-scan direction to six different locations, beginning with 331 and ending with 336, and then the sequence is repeated at 337. In FIG. 3, the offsets of locations 331-336 in the sub-scan direction are not a linear function of the main scan direction. In other words, the array 350 is  
10 not simply linearly scanned in the sub-scan direction. Rather, it jumps around to different locations as the main sweep progresses. The result is an irregular pattern of spots, as shown in FIG. 3, as compared to the regular pattern of FIG. 2.

[0022] One advantage of irregular patterns is that, compared to regular patterns, they are less likely to result in visible artifacts. In addition, an irregular pattern increases the distance  
15 between adjacent spot arrays. For example, the spots in arrays 331 and 332 are further separated than the spots in arrays 231 and 232. This increases the time between the generation of spots that are close to each other (e.g., arrays 331 and 333), thus allowing more cooling between exposures. Irregular patterns can also result in more uniform two-dimensional coverage. In FIG. 2, the resulting pattern is a set of parallel diagonal lines, where the spot  
20 coverage is densely grouped in the direction along the lines and sparsely grouped in the orthogonal direction. In FIG. 3, the spot density is more uniform over all directions.

[0023] FIGS. 2 and 3 are merely two examples of arrays and patterns. Other variations will be apparent. For example, both FIGS. 2 and 3 used a basic dither sequence (231-234 in FIG. 2, and 331-336 in FIG. 3) that was repeated. Non-periodic or random/quasi-random  
25 dither sequences can also be used.

[0024] As another example, the array of light beams can take different shapes. The examples in FIGS. 2 and 3 can be straightforwardly extended from 1xN arrays of light beams to a rectangular mxn array of light beams, where there would be n rows of m light beams each and the travel in the sub-scan direction would be approximately equal to (or less than) the row-  
30 to-row spacing. The examples in FIGS. 2 and 3 can be considered to be an array of n rows with 1 light beam in each row. The array can also be non-rectangular in shape. It can be based



on a grid with non-orthogonal coordinates (e.g., a hexagonal grid) or not even be grid-based at all. For example, the array could contain a number of light beams that were irregularly or non-uniformly distributed, so long as the resulting array was elongated in the sub-scan direction.

[0025] As used in this application, the term spot is meant to refer to a treatment location within a treatment area, for example a region on the patient's skin in a dermatological application, to which a light beam is directed in order to treat that location. The exposure of the light beam on the location typically can be varied in duration and/or intensity and the resulting exposure creates the spot within the treatment area. After a spot is created, the light beam typically is moved to a different location to create another spot. In this way, successive movement of the light beams over many locations results in treatment of the treatment area. The end result is a two-dimensional pattern of spots or, in some cases, a three-dimensional pattern depending on how deep the optical energy penetrates.

[0026] FIG. 4 is a block diagram of a light treatment apparatus for generating an array of light beams according to the invention. The apparatus includes an optical module 410, either with or without an optical source 415, and a sub-scan module 420. The apparatus optionally also includes a main scan module 430, a main scan sensor 440 and/or input/output 450. A controller 490 is coupled to the different components as applicable.

[0027] The apparatus operates as follows. The optical module 410 generates the array of light beams that is used to form the pattern of spots. The sub-scan module 420 is coupled to the optical module 410 and dithers the array of light beams in the sub-scan direction, as described above. The main scan module 430 is also coupled to the optical module 410 and sweeps the array of light beams along the main scan direction. If the apparatus does not do the sweeping (e.g., if the physician manually sweeps the array), then there is no need for a main scan module 430. The main scan sensor 440, if present, senses motion of the array of light beams along the main scan direction and this information can be used different purposes, as described below. The input/output 450 is conventional. Examples include a touch screen, keypad, liquid crystal display, electrical connector, wireless connection, etc.

[0028] Referring to each of the components in more detail, the optical module 410, which generates the array of light beams, can be implemented in a number of different ways. If the optical module 410 includes an optical source 415, then the array of light beams can be generated from the output of the optical source 415. Alternately, the optical module 410 may

not have its own optical source 415. Rather, the optical module 410 could include an optical input port (e.g., an optical fiber) that receives an input light beam(s) from an external source. Optics within the optical module 410 then generate the outgoing array of light beams from the input light beam(s).

5 [0029] In addition, the light beams in the array can be generated simultaneously. For example, a single light beam can be optically split into multiple beams, all of which are simultaneously on or off. Examples of optical splitters include fiber optic splitters, integrated waveguide splitters, gratings, diffractive elements, multi-faceted optical components (i.e., with different regions, each of which is illuminated and directs a portion of the light beam to a  
10 different location) and free space beamsplitters.

[0030] Alternately, the light beams can be generated sequentially in time. For example, a light deflecting module can deflect a light beam to the first position in the array, then to the second position, then to the third, etc. Examples of light deflectors include scan mirrors (i.e., galvanometers), acousto-optic devices, and rotating optical elements (e.g., with facets that are  
15 sequentially illuminated as each facet rotates through the optical beam). The two approaches can also be combined. For example, three light beams may be sequentially deflected to each of four different positions to create an array with twelve light beams.

[0031] The array of light beams can also be generated from multiple sources. Each source can be used to generate one of the light beams in the array. For example, an array of  
20 laser diodes can be imaged onto the treatment area to form the array of light beams. In fact, multiple sources can even be combined to form each of the light beams in the array. In one approach, different sources are coupled into the optical module 410 by fiber bundles, with at least three fibers of uniform size in a bundle. Each fiber bundle generates one of the light beams in the array.

25 [0032] The wavelengths of the light beams depend in part upon the application (e.g., the type of dermatological condition to be treated). Lasers having different wavelengths are used in surgical applications such as dermatology. Examples of laser light sources include diode lasers, diode-pumped solid state lasers, Er:YAG lasers, Nd:YAG lasers, argon-ion lasers, He-Ne lasers, carbon dioxide lasers, excimer lasers, erbium fiber lasers, and ruby lasers. These  
30 devices generate laser beams having the wavelength in the visible range of the spectrum (0.4-0.7  $\mu\text{m}$ ) as well as in infrared (0.7-11  $\mu\text{m}$ ) and UV (0.18-0.40  $\mu\text{m}$ ) ranges. It should be noted

that terms such as “optical” and “light” are meant to include all of these wavelength regions and not just the visible range of the spectrum. Candela Laser Corp. of Wayland, MA, Coherent, Inc. of Santa Clara, CA and other manufacturers market these types of lasers.

[0033] The optical source could include one particular type of laser light source capable of providing one wavelength or a wavelength range. Alternatively, the optical source could include two or more different types of laser light sources to provide a variety of different wavelengths or wavelength ranges. Light beams from different laser light sources can be directed to the treatment area either simultaneously or sequentially. For example, see co-pending U.S. Patent Application Ser. No. 10/017,287, “Multiple Laser Treatment,” filed on Dec. 12, 2001 and incorporated by reference herein.

[0034] For certain embodiments, the optical source is desirably a diode laser, such as an infrared diode laser. For other embodiments, the optical source is desirably a fiber laser, such as an erbium fiber laser manufactured by IPG Photonics of Oxford, MA. However, while lasers are the preferred embodiment of the optical source described here, other optical sources such as a flashlamp can also be used.

[0035] Referring now to the sub-scan module 420, the optical module 410 generates the array of light beams and the sub-scan module 420 dithers the array in the sub-scan direction. These two modules are shown as separate in FIG. 4, but this is purely for illustrative purposes. In actual implementations, the two modules may be separate, or they may be integrated together. In an example where the two are separate, the optical module 410 can be upstream of the sub-scan module 420 in the optical train. The optical module 410 generates the array of light beams; the sub-scan module 420 receives the array and then dithers the array of light beams. Alternatively, the sub-scan module 420 can be upstream of the optical module 410. For example, the sub-scan module 420 can dither an incoming light beam; the optical module 410 receives the dithered light beam and splits it into the array of light beams. The two modules can also be integrated together. For example, if a single galvanometer with a diffractive grating for the reflective element is used to both generate the array of light beams by diffraction, and also to implement the dither function, then the two modules effectively are implemented as a single unit. For convenience, the two modules are described as being “coupled” to each other. This is intended to be interpreted broadly, including all of the configurations described above. Similar remarks apply to other components that are “coupled” to each other.

[0036] The sub-scan module 420 can be implemented in a number of different ways. Conventional techniques for dithering a light beam or an array of light beams can be used. For example, the optical source generating the array or other components within the optical train can be physically moved, for example by mounting the components on a slide or a movable carriage. Alternately, the light beams can be dithered by optically deflecting the beams. Scan mirrors (i.e., galvanometers), acousto-optic devices, and rotating optical elements are some examples.

[0037] The optional main scan module 430 sweeps the array of light beams along the main scan direction. The underlying function (steering light beams) is similar to that of the sub-scan module 420, although the total travel and desired speed may be significantly different. Thus, the same conventional approaches are also candidates for the main scan module, although the actual implementation may be significantly different due to the travel and speed considerations. For example, both sweeping and dithering may be implemented by physical translation. But the main scan module 430 may sweep across several inches or feet at a moderate speed; whereas the sub-scan module 420 dithers across a fraction of an inch at much higher speeds. Thus, the main scan module 430 may be implemented by a robotic arm that holds the hand piece of the apparatus; whereas the sub-scan module 420 may be implemented by a small carriage mounted on rails, located internal to the hand piece.

[0038] The main scan sensor 440 senses the sweeping motion and can be implemented in different ways. For example, the main scan sensor 440 can measure relative position or velocity, similar to the mechanisms used in certain types of computer mouse. Alternately, it can measure absolute position, using triangulation from known beacons, or GPS or similar systems.

[0039] The information gathered by the main scan sensor 440 can be used for different purposes. The information can be used as feedback to control automated sweeping by the main scan module 430, or can also be used to control or coordinate the dithering by the sub-scan module 420. For example, if the physician sweeps at an uneven speed, then the dithering speed can be automatically adjusted to match the physician's sweep speed. For example, see co-pending U.S. Patent Application Ser. No. xxx [attorney docket number 8533], "Method And Apparatus For Monitoring and Controlling Laser-Induced Tissue Treatment," filed on December 23, 2003 and incorporated by reference herein.

[0040] The controller 490 may be used to control the placement, intensity, duration and other characteristics of the light beams in order to generate the spots on the treatment area. The controller 490 can be implemented in many different forms: for example, electromechanical systems, dedicated electronic circuitry, ASIC, microprocessor, programmable DSPs, software, or combinations of the above. The controller 490 communicates with the different components 410-450, as applicable. In general, a controller may respond to preprogramming or operator activation (e.g., via the input/output 450).

[0041] Control parameters can be used to specify the location of each spot in the pattern; the dither amounts and/or dither sequence for the array of light beams in the sub-scan direction; when to line feed in the main scan direction (i.e., reset to the beginning of the next sweep); the intensity of the light beams to be generated; the duration of the illumination; and/or when to turn on or off a particular light beam in the array (individual beams can be turned on and off independently in some embodiments). Thus, the control parameters can be used to specify the amount of exposure commensurate with a treatment goal. The control parameters can be hard wired. Alternately, an operator may program the control parameters, for example via the input/output 450. In an embodiment, these control parameters are stored in the memory.

[0042] For purposes of non-ablative coagulation of a dermal layer of the treatment area, a laser light source can provide an optical beam having a wavelength of approximately 1.5  $\mu\text{m}$  and an optical fluence incident on the outer surface of the skin between approximately 0.1 Joules/cm<sup>2</sup> and 100,000 Joules/cm<sup>2</sup>, such as between approximately 1 Joules/cm<sup>2</sup> and 1000 Joules/cm<sup>2</sup>. For certain applications, the pulse duration of an optical beam can be approximately equal to or less than a thermal diffusion time constant, which is approximately proportional to the square of the diameter of the focal spot within the treatment area. Pulse durations that are longer than the thermal diffusion time constant can be less efficient and cause the spot to undesirably grow or shrink by thermal diffusion. It should be noted that the light beams might accomplish the goal of completely treating the treatment area in one pass or in multiple passes.

[0043] FIG. 5 is a diagram of one implementation of a light treatment apparatus using a single light source. In this example, the optical source is based on an Erbium fiber laser 515, which has a wavelength of 1.54  $\mu\text{m}$ . The laser 515 is driven by a pulse source 512. The

controller 590 adjusts the timing and duration of the pulses to control the exposure of the spots 575 in the treatment area 570. The light beam from the fiber laser 515 is delivered through a single-mode fiber 516 to the hand piece 580. A collimating lens 517 collimates the output from the single-mode fiber 516. A beamsplitter 519 divides the collimated beam into two collimated beams of roughly equal power. In alternate embodiments, additional optics can be used to generate additional beams. A focusing lens 562 focuses each collimated beam to a spot 575 within the skin 570. A flat sapphire plate 564 is in contact with the skin. It serves as an optical window for the hand piece 580 and also allows the light beams to be focused to the same depth within the skin for each of the beams. In this example, the array of light beams is a 1xN array and is about 1 cm long in the sub-scan direction. The window 564 is slightly larger. The optical components preferably are anti-reflection coated to maximize the optical power that is coupled into the skin.

**[0044]** Additional optics 520 between the collimating and focusing elements 517 and 562 dither the location of the multiple light beams on the surface of the skin. In this implementation, optical elements 520 are rotated by motors in the hand piece. Each optical element is divided into different facets, each of which dithers the light beams by different amounts. When the elements are rotated, the array of light beams is sequentially dithered to the different locations, thus generating the pattern of spots. For example, see co-pending U.S. Patent Application Ser. No. xxx [attorney docket number 8534], "High Speed, High Efficiency Optical Pattern Generator using Rotating Optical Elements," filed on even date herewith and incorporated by reference herein.

**[0045]** The user can adjust the distance between adjacent spots in the treatment pattern according to the desired treatment level. In addition, selected spots within the pattern can be turned off if a larger range of treatment levels is desired. A velocity sensor in the tip of the hand piece measures the speed of the hand piece as it moves across the treatment area. If the user changes the velocity of the hand piece across the skin, the controller 590 adjusts the rate at which the apparatus generates spots.

**[0046]** FIG. 6 is a diagram of another implementation of a light treatment apparatus using multiple light sources. In this example, five diode lasers 615 are coupled into high brightness glass fiber pigtailed 617. The pigtailed are arranged to form a 1xN array ( $N=5$ ). Each of the diode lasers 615 provides 1 W of continuous or pulsed power. Higher or lower power optical sources can be used. Some industrial systems can be purchased with a thermoelectric

cooler, heat sink, fan, power supply and component electronics all in one package. The fibers 617 are terminated with an epoxy-free industry standard connector 620 for high power lasers to which an optional commercially available collimating lens adapter 630 can be attached and passively aligned. This arrangement can be used to produce an array 640 of closely spaced  
5 light beams of about the same size and intensity. Customized optics and/or housings can be used to achieve a closer spacing. The fiber pigtails are mounted on a carriage 620 that is moveable in the sub-scan direction 622. A motor drives the carriage, thus dithering the array of light beams in the sub-scan direction.

[0047] Although specific embodiments of the invention have been described with

10 reference to the drawings, it should be understood that the embodiments shown are by way of examples only and merely illustrative of but few of many possible specific embodiments, which represent application of the principles of the invention. For example, there is no need for a mechanical device or a carriage to sweep the laser beam over a treatment area in the main scan direction. This can be accomplished using a manual method, such as a hand piece that a  
15 physician or other operator moves over a treatment area. As another example, the transverse sub-scan direction can make angles other than 90 degrees with respect to the main scan direction. For example, for spots placed on a hexagonal grid pattern, the transverse sub-scan direction may be at 60 degrees to the main scan direction. Another common angle that can be used is 75 degrees. Various changes and modifications obvious to one skilled in the art to  
20 which the invention pertains are deemed to be within the spirit, scope and contemplation of the invention as further defined in the appended claims. Furthermore, no element, component or method step is intended to be dedicated to the public regardless of whether the element, component or method step is explicitly recited in the claims.

WHAT IS CLAIMED IS:

1. A light treatment apparatus for generating a pattern of spots over a treatment area, comprising:

an optical module for generating an array of light beams, wherein the array is elongated  
5 along a sub-scan direction that is transverse to a main scan direction; and  
a sub-scan module coupled to the optical module for dithering the array of light beams  
in the sub-scan direction; wherein, for a sweep of the array along the main scan  
direction, a travel of the array in the sub-scan direction is not more than a length  
of the array in the sub-scan direction.

10 2. The apparatus of claim 1 wherein the optical module comprises:  
a fiber coupled laser diode.

3. The apparatus of claim 1 wherein the optical module comprises:  
a fiber laser.

4. The apparatus of claim 1 wherein the optical module comprises:  
15 a laser for generating a laser beam; and  
optics coupled to the laser for generating the array of light beams from the laser beam.

5. The apparatus of claim 1 wherein the optical module comprises:  
a plurality of light sources; and  
optics coupled to the light sources for generating the array of light beams from the  
20 plurality of light sources.

6. The apparatus of claim 1 wherein the optical module comprises:  
an optical input port for receiving one or more input light beams from an external  
source; and  
optics coupled to the optical input port for generating the array of light beams from the  
25 received input light beams.

7. The apparatus of claim 6 wherein the optical input port comprises an optical fiber.

8. The apparatus of claim 1 wherein the optical module generates all of the light beams  
simultaneously.



9. The apparatus of claim 1 wherein the optical module generates the light beams sequentially in time.

10. The apparatus of claim 1 wherein the sub-scan module comprises:  
a movable carriage that can be translated in the sub-scan direction.

5 11. The apparatus of claim 1 wherein the sub-scan module comprises:  
a light deflecting module configured to deflect one or more of the light beams.

12. The apparatus of claim 1 wherein the array of light beams is a rectangular array of light beams with N rows in the sub-scan direction.

13. The apparatus of claim 12 wherein  $N > 2$ .

10 14. The apparatus of claim 13 wherein the travel in the sub-scan direction is not more than a row-to-row spacing in the sub-scan direction.

15. The apparatus of claim 1 wherein the array of light beams is a  $1 \times N$  array of light beams.

15 16. The apparatus of claim 1 wherein the array of light beams has a length of about 1 cm in the sub-scan direction.

17. The apparatus of claim 1 wherein the sub-scan direction is perpendicular to the main scan direction.

18. The apparatus of claim 1 wherein the travel of the array in the sub-scan direction is less than one half of the length of the array in the sub-scan direction.

20 19. The apparatus of claim 1 further comprising:  
a main scan module coupled to the optical module for automatically sweeping the array of light beams along the main scan direction.

20. The apparatus of claim 1 further comprising:  
a controller for adjusting a location and/or an exposure of the light beams to generate  
25 the pattern of spots.

21. The apparatus of claim 20 wherein the pattern of spots produces fractional phototherapy of the treatment area.

22. The apparatus of claim 20 wherein the pattern of spots is an irregular pattern of spots.

23. The apparatus of claim 20 wherein the controller is coupled to the sub-scan module for controlling the dithering of the array of light beams to generate the pattern of spots.

24. The apparatus of claim 20 further comprising:

a main scan sensor for sensing the sweeping of the array of light beams along the main scan direction, wherein the controller is coupled to the sub-scan module and the main scan sensor and controls dithering of the array in response to sweeping of the array.

25. A method for generating a pattern of spots over a treatment area, comprising:

generating an array of light beams, wherein the array is elongated along a sub-scan direction;

sweeping the array of light beams along a main scan direction that is transverse to the sub-scan direction; and

for a sweep of the array along the main scan direction, automatically dithering the array in the sub-scan direction, wherein a travel of the array in the sub-scan direction is not more than a length of the array in the sub-scan direction and the sweeping along the main scan direction and the dithering in the sub-scan direction generate the pattern of spots.

26. The method of claim 25 wherein the step of generating an array of light beams comprises:

generating all of the light beams simultaneously.

27. The method of claim 25 wherein the step of generating an array of light beams

comprises:

generating the light beams sequentially in time.

28. The method of claim 25 wherein the array of light beams is a rectangular array of light beams with N rows in the sub-scan direction.

29. The method of claim 28 wherein the travel in the sub-scan direction is not more than a row-to-row spacing in the sub-scan direction.

30. The method of claim 25 wherein the step of sweeping the array of light beams along a main scan direction comprises:

5 automatically sweeping the array of light beams along the main scan direction.

31. The method of claim 25 wherein the step of sweeping the array of light beams along a main scan direction comprises:

manually sweeping the array of light beams along the main scan direction.

32. The method of claim 25 further comprising:

10 adjusting an exposure of the light beams in the array.

33. The method of claim 25 wherein the pattern of spots produces fractional phototherapy of the treatment area.

34. The method of claim 25 wherein the pattern of spots is an irregular pattern of spots.

35. The method of claim 25 wherein the step of automatically dithering the array of light  
15 beams in the sub-scan direction comprises:

sensing sweeping of the array along the main scan direction; and

controlling dithering of the array in response to the sensed sweeping of the array along  
the main scan direction.

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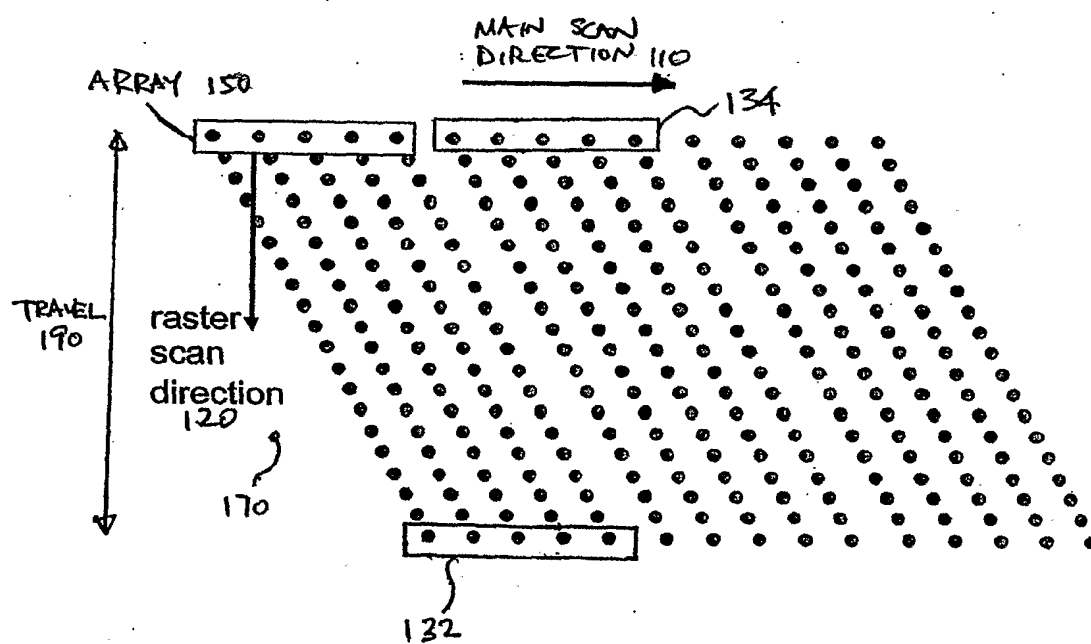


FIG. 1

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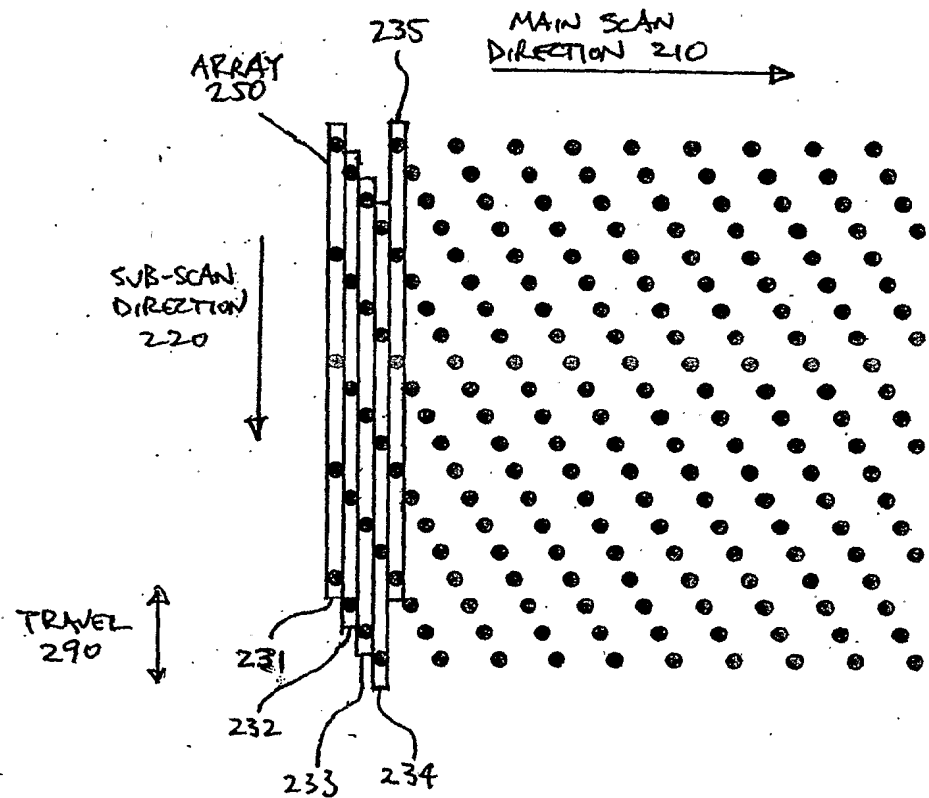


FIG. 2

3/6

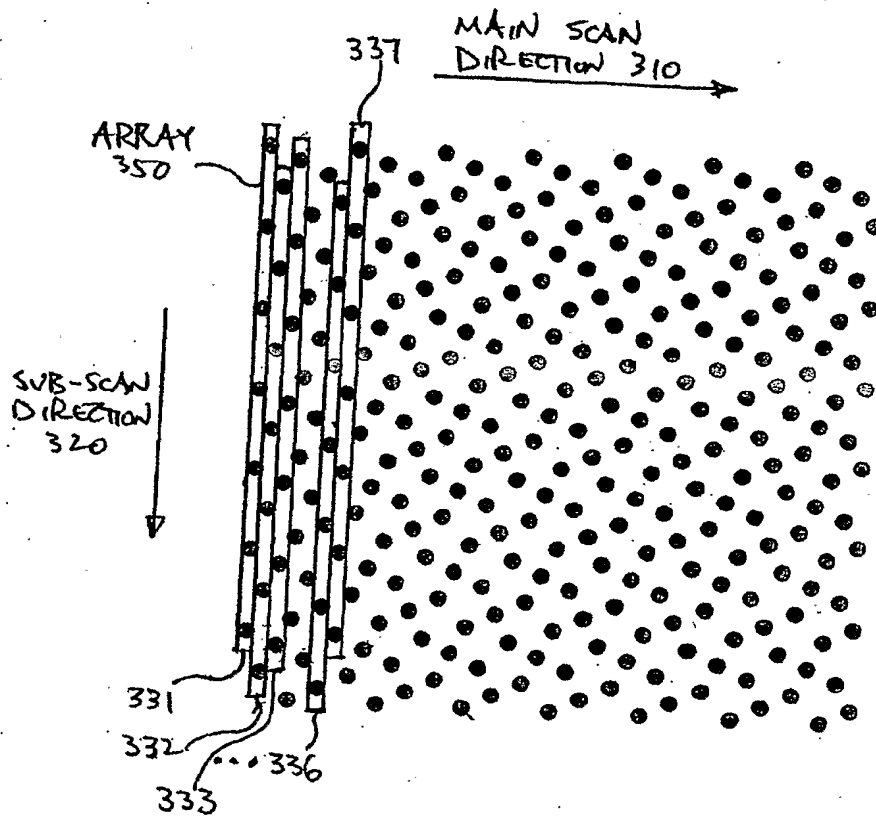


FIG. 3

4/6

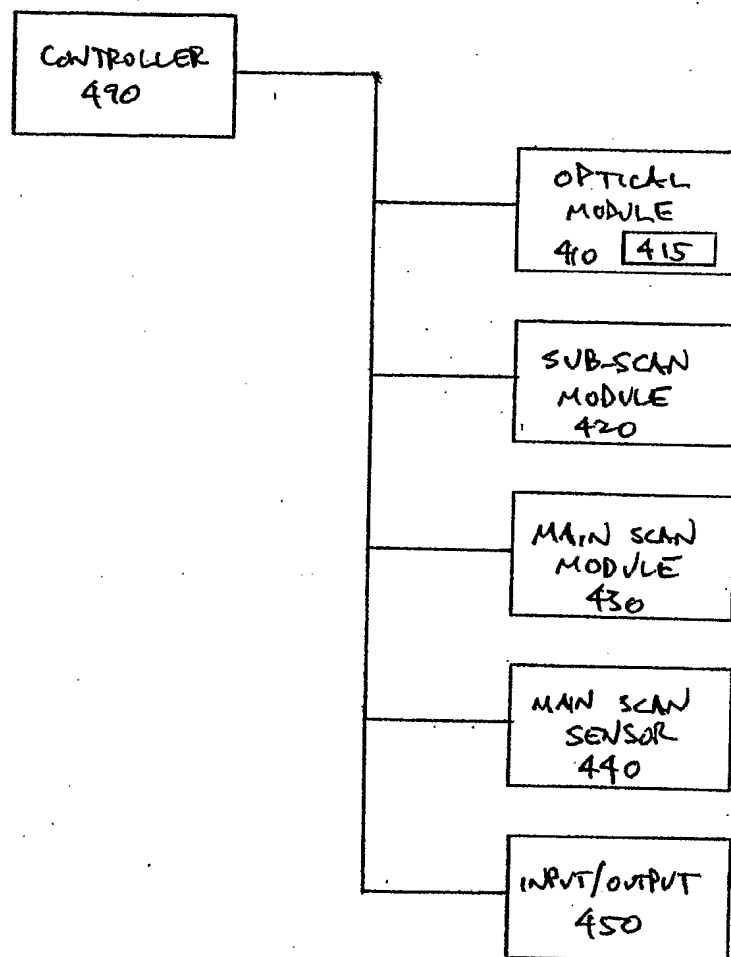


FIG. 4

5/6

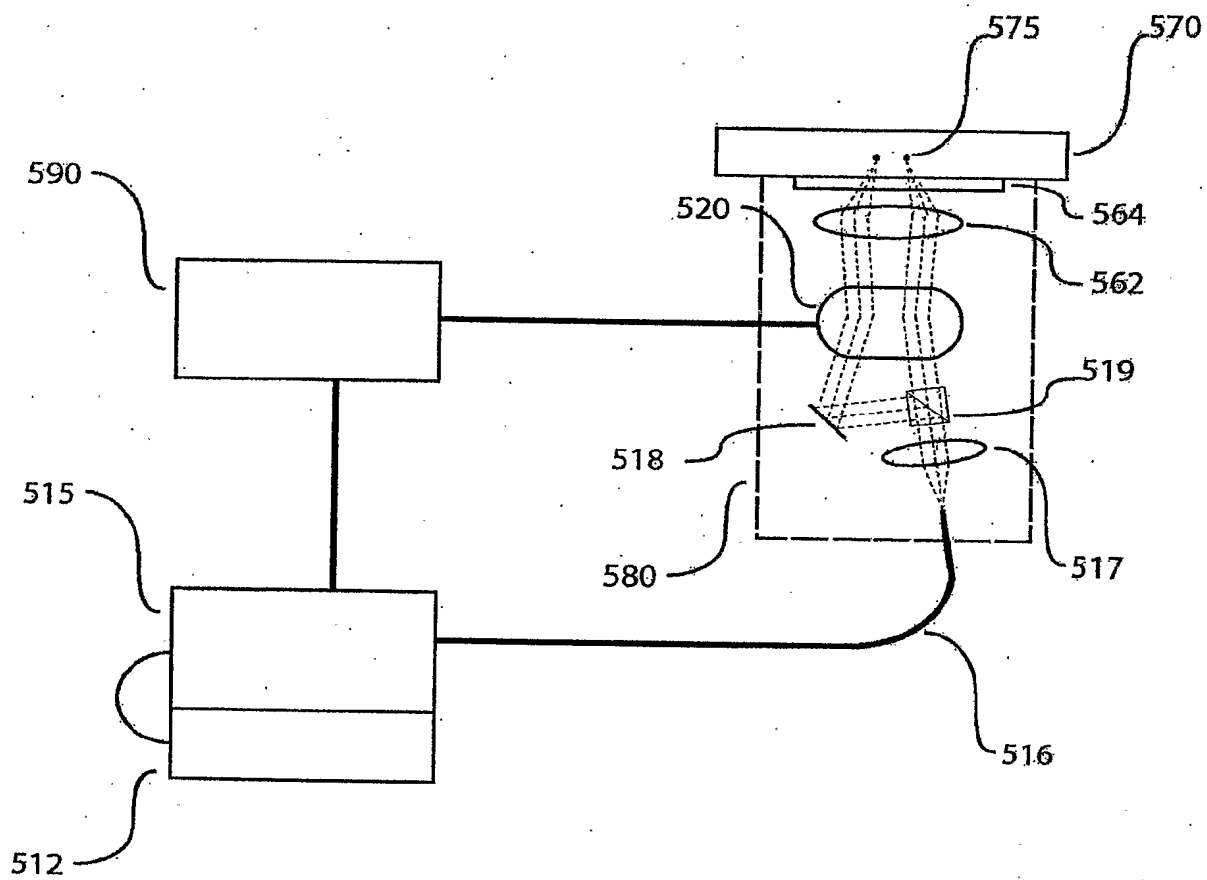


FIG. 5



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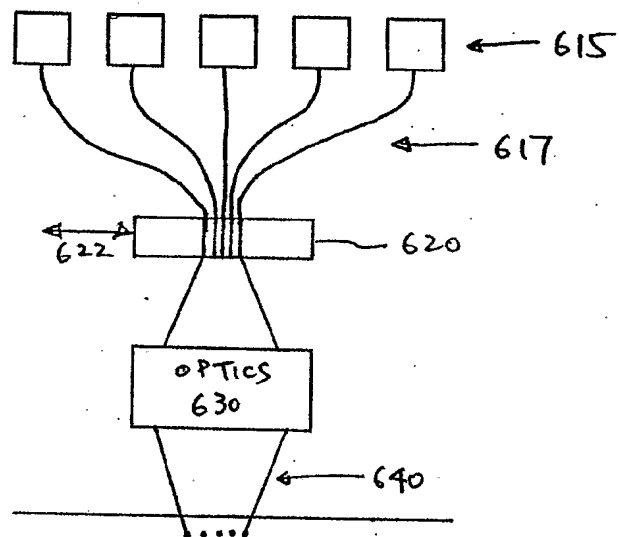


FIG. 6

## TREATMENT DEVICE

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**Inventor(s):** YAMAZAKI IWAO [JP]

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**Classification:**

- **international:** **A45D26/00; A61B18/20; A61B19/00; A61N5/06; A61N5/067; A45D26/00; A61B18/20; A61B19/00; A61N5/06; (IPC1-7): A61N5/06; A45D26/00; A61B18/20**

- **European:** A61B18/20H

**Application number:** WO2005JP05282 20050323

**Priority number(s):** JP20040093892 20040326

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JP2002355320 (A)

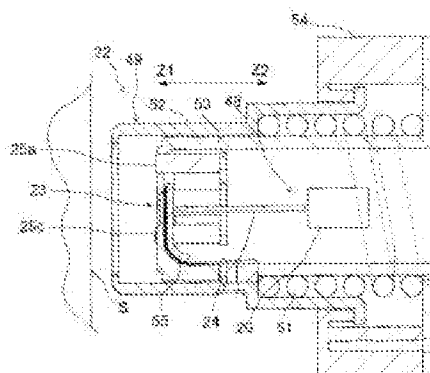
JP2002306230 (A)

JP59228862 (A)

JP2000334052 (A)

### Abstract of WO 2005092438 (A1)

A treatment device comprises a laser light radiating mechanism consisting of a laser drive circuit for radiating laser light from a laser radiation port onto a skin surface which is a subject of treatment, a laser diode, and a light guide lens, a shield member (shutter) for opening/closing a laser radiation port on the basis of the distance between the skin surface and the laser radiation port, and a sleeve-like member covering the laser radiation port, adapted to actuate the shield member, and capable of advance and retraction. Further, disposed at positions surrounding the laser radiation port inside the sleeve-like member are three contacts for realizing a touch sensor function.



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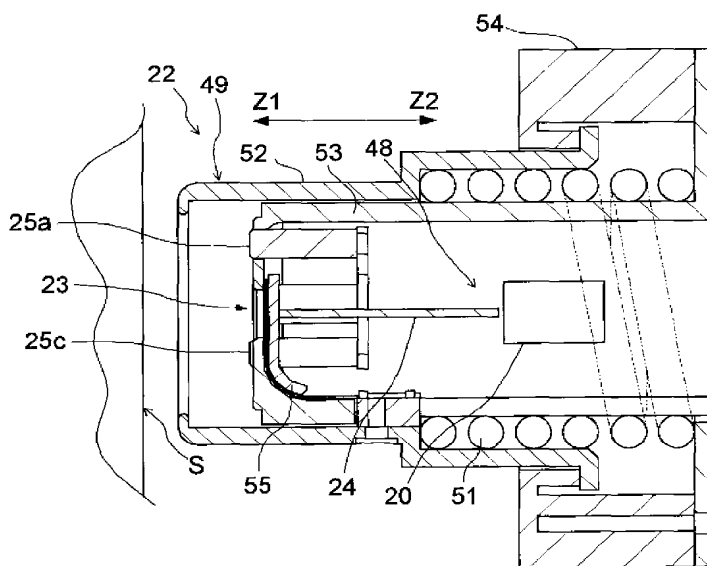
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(54) Title: TREATMENT DEVICE

(54) 発明の名称: トリートメント装置



(57) Abstract: A treatment device comprises a laser light radiating mechanism consisting of a laser drive circuit for radiating laser light from a laser radiation port onto a skin surface which is a subject of treatment, a laser diode, and a light guide lens, a shield member (shutter) for opening/closing a laser radiation port on the basis of the distance between the skin surface and the laser radiation port, and a sleeve-like member covering the laser radiation port, adapted to actuate the shield member, and capable of advance and retraction. Further, disposed at positions surrounding the laser radiation port inside the sleeve-like member are three contacts for realizing a touch sensor function.

(57) 要約: 本発明のトリートメント装置は、トリートメント対象の皮膚面にレーザ光をレーザ照射口より照射するためのレーザ駆動回路、レーザダイオード、及び導光レンズなどからなるレーザ光照射機構と、皮膚面とレーザ照射口との離間距離に基づいて

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LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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レーザ照射口を開閉するための遮蔽部材（シャッター）と、レーザ照射口を包囲するとともに、遮蔽部材を動作させる進退移動自在な筒状部材等とを備える。さらに、筒状部材の内側のレーザ照射口を包囲する位置には、タッチセンサ機能を実現するための三つの接触子が配置されている。

## 明 細 書

### トリートメント装置

### 技術分野

- [0001] 本発明は、レーザ光などの光を皮膚面に照射して美容処理を施すためのトリートメント装置に関する。

### 背景技術

- [0002] 一般に、エネルギー密度の高いレーザ光を皮膚面に照射して皮膚の生体組織を加温することなどで、皮膚の細胞組織の活性化を図り、美肌や育毛などのトリートメントを行えるレーザ光照射型のトリートメント装置が知られている(例えば、特許文献1参照)。
- [0003] この種のトリートメント装置では、皮膚面へ照射されるレーザ光のパワーや照射時間などを適宜設定することで、上記美肌処理や育毛に加え、脱毛や痩身などのトリートメントを行うことも可能である。
- [0004] ところで、このようなレーザ光照射型のトリートメント装置では、身体における意図しない部位にエネルギー密度の高いレーザ光が誤って照射されることを防止するために、タッチセンサ機能を備える装置も利用されている。すなわち、このタッチセンサ機能は、例えばレーザ光の照射口の近傍からレーザ光の照射方向に突設された例えば単一又は二つの接触子と、トリートメント対象の皮膚面との接触／非接触を検出し、レーザ光源からのレーザ光の放射／非放射を制御するものである。
- [0005] しかしながら、上記した構成のタッチセンサ機構では、レーザ光の誤照射を防止するための安全装置としては、必ずしも十分であるとはいえず、安全性の面でのさらなる向上が求められている。

特許文献1:特開2002-355320

### 発明の開示

- [0006] そこで本発明は、このような課題を解決するためになされたもので、意図しない光の照射をより確実に防止することで、トリートメントを行う際の安全性を高めることができるトリートメント装置の提供を目的とする。

- [0007] 上記目的を達成するために、本発明に係るトリートメント装置は、トリートメント対象の皮膚面に向けて照射口より光を照射する光照射機構と、前記皮膚面と前記照射口との離間距離に基づいて前記照射口を開閉する照射口開閉機構とを具備することを特徴とする。
- [0008] すなわち、この発明では、前記皮膚面と前記照射口との離間距離に基づいて、照射口が開閉されるので、例えば皮膚面に照射口が近接した場合に照射口を開放し、一方、皮膚面から照射口が比較的遠くに離間した場合に照射口を閉塞させることなどが可能である。これにより、トリートメントを行うべき所望の皮膚面と光の照射口とが所定の距離内に近接してはじめて光の照射が可能となる。したがって、本発明によれば、意図しない光の照射をより確実に防止できるので、照射口より放出される光が、例えばエネルギー密度の高いレーザ光などである場合でも、トリートメントを行う際の安全性を高めることができる。
- [0009] また、本発明に係るトリートメント装置は、前記照射口開閉機構が、前記照射口を周縁から包囲するとともに先端部が前記照射口から突出する前進位置と前記前進位置から後退する所定の後退位置との間を進退移動自在に設けられた筒状部材と、前記筒状部材の進退移動に連動し前記筒状部材が前記前進位置に移動した場合に前記照射口を閉塞し、前記筒状部材が前記後退位置に移動した場合に前記照射口を開放する遮蔽部材と、前記筒状部材を前記前進位置に付勢する付勢部材とを具備することを特徴とする。
- [0010] すなわち、この発明では、筒状部材の先端部を皮膚面に押圧して、付勢部材の付勢力に抗しつつこの筒状部材が後退位置に後退した場合にのみ遮蔽部材が移動して照射口が開放し、光が皮膚面に照射される。一方、筒状部材の先端部を皮膚面に押圧していない場合、付勢部材の付勢力によって筒状部材が前進位置に定位し遮蔽部材も移動しないことになるから、照射口の閉塞状態が維持され皮膚面への光の照射が阻止される。したがって、この発明においても、トリートメントを行うべき皮膚面と光の照射口とが所定の距離内に近接してはじめて光の照射が可能となるので、意図しない光の照射を防止することができる。
- [0011] さらに、本発明に係るトリートメント装置は、前記筒状部材の内側から前記照射口を

包囲するように配置された少なくとも3つ以上の接触子と、前記各接触子と前記皮膚面との接触を検出して前記光照射機構を作動させるタッチセンサ機構とを具備することを特徴とする。

[0012] この発明では、上記した筒状部材が前進位置に位置する場合、つまり筒状部材の先端部が皮膚面に押圧されていない非トリートメント時では、遮蔽部材が照射口を閉塞し、しかも各接触子も筒状部材に覆われるので、トリートメント時以外に誤って光が放射されてしまうことが抑制される。つまり、この発明では、筒状部材の後退動作と、各接触子の皮膚面への接触動作との二つの動作が共に行われてはじめて光が照射される二重のプロテクト機能を備えているので、トリートメントを行う際の安全性をより高めることができる。また、このような安全性の高い光照射の防止機能は、光照射機構によって照射される光が、エネルギー密度の高いレーザ光などである場合に有用である。

[0013] また、この発明では、皮膚面との接触状態／非接触状態の直接的検出部分である接触子が、三つ以上設けられ、しかも光の照射口を包囲する位置に実質的に分散されたかたちで配置されることになるので、光の照射口の向きが確実に定まり、トリートメントを行うべき所望の皮膚面と光の照射口とが完全に対向してはじめて光が照射されることになる。

[0014] さらに、本発明に係るトリートメント装置は、前記光照射機構が、光源と、前記光源から放出された光を集光する光学系とを備え、さらに、前記光学系により集光される光の焦点位置が、前記各接触子の前記皮膚面との接触部分よりも、前記光源側に位置することを特徴とする。

[0015] この発明では、光の焦点位置が、皮膚面上に重なるおそれがなく、皮膚面上には焦点位置を越えて、再び放散されるエネルギー密度の低下した光が照射されるので、トリートメントを行う際の安全性が確保される。

[0016] また、本発明のトリートメント装置は、前記筒状部材が前記後退位置に移動したことを検出する検出手段と、前記検出手段により前記筒状部材の前記後退位置への移動が検出されない状態では、前記光照射機構の駆動を阻止する光照射阻止手段と、をさらに具備することを特徴とする。

[0017] さらに、本発明のトリートメント装置は、前記光源から放出された光を入射しこの入射した光の断面形状の縦横比を変化させつつ当該光を出射するレンズを備えることを特徴とする。また、前記レーザ照射口は、前記レンズを通過した光の断面形状の縦横比に対応させた例えば矩形状の穴により形成されていることが好ましい。また、前記レンズにおける光の入射面及び出射面となる部位は、例えば、縦横の曲率が異なるように膨出させた形状で形成される。

### 図面の簡単な説明

- [0018] [図1]本発明の実施形態に係るトリートメント装置を示す斜視図。  
[図2]図1のトリートメント装置が備えるレーザ照射装置を示す正面図。  
[図3]図2のレーザ照射装置を側面からみた断面図。  
[図4]図2のレーザ照射装置のヘッド部を示す斜視図。  
[図5]図4のヘッド部のレーザ光の非照射時の状態を側面からみた断面図。  
[図6]図4のヘッド部のレーザ光の照射時の状態を側面からみた断面図。  
[図7]図1のトリートメント装置の制御系を機能的に示すブロック図。  
[図8]図7の制御系の一部を構成するタッチセンサ回路を機能的に示すブロック図。  
[図9]図6のヘッド部と構造の異なる他のヘッド部を示す図。  
[図10]図6、図9のヘッド部と構造の異なる他のヘッド部を示す図。  
[図11]図6、図9、図10のヘッド部と構造の異なる他のヘッド部を示す斜視図。  
[図12]図11のヘッド部を示す平面図。  
[図13]図11のヘッド部に内蔵された光学系を模式的に示す斜視図。  
[図14]図6、図9、図10、図11のヘッド部と構造の異なる他のヘッド部を示す斜視図。  
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[図15]図14のヘッド部を示す平面図。

### 発明を実施するための最良の形態

- [0019] 以下、本発明の実施の形態を図面に基づき説明する。
- [0020] 図1は、本発明の第1の実施形態に係るトリートメント装置を示す斜視図、図2は、このトリートメント装置が備えるレーザ照射装置を示す正面図である。また、図3は、図2のレーザ照射装置を側面からみた断面図、図4は、このレーザ照射装置のヘッド部を



示す斜視図である。さらに、図5は、図4のヘッド部のレーザ光の非照射時の状態を側面からみた断面図、図6は、図4のヘッド部のレーザ光の照射時の状態を側面からみた断面図である。また、図7は、図1のトリートメント装置の制御系を機能的に示すブロック図、図8は、図7の制御系の一部を構成するタッチセンサ回路を機能的に示すブロック図である。

- [0021] 図1に示すように、このトリートメント装置1は、ユーザが自身で操作する美容処理装置であって、コントローラ兼器具収容ボックス(以下、「コントロールボックス」と称する)2と、このコントロールボックス2に接続ケーブル3を通じて接続されたレーザ照射装置5とから構成される。
- [0022] コントロールボックス2の前面には、トリートメント装置本体を操作するための案内情報や装置の動作状態などが視覚的に表示される表示パネル6と、接続ケーブル3の接続端子(プラグ)を取り付けるソケット7などが設けられている。また、コントロールボックス2には、レーザ照射装置5へ電力を供給するための電源や、レーザ照射装置5からのレーザ光の照射を制御する制御回路が内蔵されている。
- [0023] さらに、このコントロールボックス2の前面には、この美容処理装置本体の電源のオン／オフを行う電源スイッチ8と、電源のオン／オフの状態を示すLED9と、各種設定を行う設定スイッチ10と、各設定状態を視覚的に示すLED11とが設けられている。
- [0024] また、図2及び図3に示すように、レーザ照射装置5は、ユーザが手で持ってトリートメントを行うハンディタイプの装置である。すなわち、レーザ照射装置5は、装置の外郭を形成するケース12と、このケース12の内部に基板15を介して搭載された制御チップ16と、ケース12の全面に設けられた設定スイッチ19と、レーザ光を放射する光源としてのレーザダイオード20と(図5、図6参照)、レーザダイオード20の熱を除去するヒートシンクと、ヒートシンクを冷却する冷却ファン17と、レーザダイオードから出射されたレーザ光を導光しつつレーザ照射口23からレーザ光を身体の皮膚面に照射する棒状の導光レンズ24とから主に構成されている。
- [0025] 設定スイッチ19は、図2に示すように、トリートメント装置本体の電源をレーザ照射装置5側でオン／オフし、LEDランプ18の点灯／非点灯によりこれをユーザに報知する。また、設定スイッチ19は、本体側の設定スイッチ10とほぼ同様の機能を有してお

り、間欠(パルス)照射されるレーザ光のオンタイム(照射時間及びその照射サイクル)を設定するためのものである。すなわち、設定スイッチ19を1回押す度に電源オン、オンタイムの切換え、電源オフの順にモードが切換わる。この際、LEDランプ18は、設定レベル1〜6に対応して緑色点灯から緑色点滅、橙色点灯、橙色点滅、赤色点灯、赤色点滅の順に表示が切換わる。また、最後に、設定スイッチ19を例えば1.5秒以上押し続けると、電源がオフとなる。

[0026] 上記したヒートシンクは、レーザダイオード20の動作時の発熱を熱伝導によって拡散させて性能の低下を抑える。このため、ヒートシンクは、熱伝導率のよいアルミニウム又はその合金等で鋳造され、また、表面積を増やすために複数の貫通孔を備え放熱効果が高められている。

[0027] レーザダイオードは、GaAs(ガリウムアルセナイド)などの化合物半導体を用いたPN接合ダイオードに直接電流を流して励起し、レーザ発振を得る。このレーザダイオード20としては、例えば波長700〜900nm、光出力5mW〜5Wのレーザ光を放射することが可能な半導体素子が適用されている。

[0028] このようなレーザ光は、光電気反応、光磁気反応、光力学反応、光化学反応、光免疫反応、光酵素反応等を誘起させる効果があり、光生物学的活性化により生体組織の新陳代謝を促して皮膚血行を高め、また、水分や血液に吸収され難いため、優れた皮膚深部への到達性を有する。

[0029] ここで、トリートメント装置1により実現可能な各種トリートメントについて簡単に説明する。

[0030] レーザ光は、他の光に比べてエネルギー密度が高いため、生体組織に照射した場合、照射部分の温度を比較的容易に上昇させることができる。これにより、レーザ光は、生体組織の所望の部位の蛋白質の変成等を意図的に引き起こさせる光熱反応や、また、代謝機能を促進するための、いわゆる非熱反応(40℃を超えない程度の比較的低い温度で起こる光化学反応、光磁気反応、イオン化反応などの生体反応)を誘起させることが可能である。

[0031] すなわちトリートメント装置1は、レーザパワーや照射時間等を適宜設定して人体の皮膚面へレーザ光を照射することで、育毛、脱毛、美肌、痩身などのトリートメントを実

現する。

- [0032] 育毛トリートメントは、エネルギー密度を比較的低く設定したレーザ光を頭皮表面に照射することで行われる。これにより、頭皮の血行が促進されて毛穴が開き、毛穴に詰まった皮脂や汚れが洗浄されることで育毛効果が得られる。一方、脱毛トリートメントは、エネルギー密度を比較的高く設定したレーザ光を体毛等の毛根に照射することで実現される。この場合、体毛等の毛母細胞の蛋白質の変成が促進されることにより、毛の成長が抑制され脱毛効果が得られる。
- [0033] また、美肌トリートメントを行う場合においては、皮膚の表皮や真皮に散在するメラニンが比較的高い温度に昇温されるようにレーザ光を照射し、光熱作用によって熱変性を引き起こさせ、アザ、シミ、ソバカスなどを除去する。また、痩身トリートメントを行う場合においては、交感神経と関連の深い特定のツボに比較的エネルギー密度の低いレーザ光を供給し、光化学反応、光磁気反応、イオン化反応等による非熱作用によってツボを刺激して血行を促し、これにより、細胞組織を活性化して代謝機能を高め余分な脂肪を燃焼させる。ここで、ヘッド部22から皮膚面に照射される対象の光をレーザ光から例えばUV光に変更してもよい。殺菌作用を有するUV光を皮膚面に照射すること等で肌の清浄化を図る殺菌トリートメントを行うことができる。
- [0034] 次に、トリートメント装置1の制御系について説明する。
- [0035] すなわち、トリートメント装置1の制御系37は、図7に示すように、各接触子25a、25b、25cの皮膚面への接触を検出しレーザダイオードからのレーザ光の放射／非放射を実質的に制御する後述のタッチセンサ回路28と、レーザ光の照射パターンが記憶されたメモリ29と、設定スイッチ10や設定スイッチ19による設定内容に応じてトリートメントのモードを切り替えるためのモード切替回路38と、レーザダイオード20を駆動してレーザ光を放射させるレーザ駆動回路30と、これらの回路を統括的に制御するCPU31と、タッチセンサ回路28及びレーザ駆動回路30とCPU31とを接続するインタフェース32等とから構成されている。
- [0036] メモリ29には、レーザダイオード20から所定の照射時間で間欠的に照射されるレーザ光の照射タイミングの設定値などを含む各種プログラムが記憶されている。レーザ駆動回路30は、CPU31の制御下でレーザダイオード20に所定の駆動電流電圧

を供給し、レーザダイオード20よりレーザ光を放射させる。

[0037] ここで、本実施形態のトリートメント装置1が備えるタッチセンサ機構について主に図3ないし図8に基づき詳述する。

[0038] すなわち、レーザ照射装置5を有するトリートメント装置1は、図3〜図6に示すように、トリートメント対象の皮膚面Sにレーザ光をレーザ照射口23より照射するためのレーザ駆動回路30、レーザダイオード20、及び導光レンズ24などからなるレーザ光照射機構48と、皮膚面Sとレーザ照射口23との離間距離に基づいてレーザ照射口23を開閉する照射口開閉機構49と、を備えている。ここで、この照射口開閉機構49は、レーザ照射口23を周縁から包囲するとともに、先端部がレーザ照射口23から(矢印Z1方向に)突出する前進位置(図5参照)と前記前進位置から(矢印Z2方向に)後退する所定の後退位置(図6参照)との間を進退移動自在に設けられた筒状部材52と、筒状部材52の進退移動に連動し筒状部材52が前進位置に移動した場合にレーザ照射口23を閉塞し(図5参照)、筒状部材52が後退位置に移動した場合にレーザ照射口23を開放する(図6参照)板バネ等で形成された遮蔽部材(シャッタ)55と、筒状部材52を前進位置に付勢する付勢部材としてのコイルスプリング51とを備える。

[0039] また、ヘッド部22には、レーザダイオード20、導光レンズ24、遮蔽部材(シャッタ)55が内蔵された内側筒体53が設けられている。つまり、レーザ照射口23は、内側筒体53の先端側に設けられている。筒状部材52は、内側筒体53の外径部分と摺動するかたちで(矢印Z1〜Z2方向に)進退移動する。コイルスプリング51は、自身の内径部分が内側筒体の外形部分にはめ込まれており、筒状部材52の段差部を通じてこの筒状部材52を(矢印Z1方向に)付勢する。筒状部材52及び内側筒体53は、台座54を通じてケースに固定される。また、上記した接触子25a、25b、25cは、レーザ照射口23からレーザ光の照射方向に突出し、且つ筒状部材52の内側からレーザ照射口23を包囲するように少なくとも三つ以上(本実施形態では三つ)配置されている。タッチセンサ回路28は、これらの各接触子(全ての接触子)25a、25b、25cと皮膚面Sとの接触を検出して、CPU31の制御下で上記レーザ光照射機構48(レーザ駆動回路30)を作動させる。

[0040] つまり、この実施形態のトリートメント装置1では、筒状部材52の先端部を皮膚面S

に押圧して、コイルスプリング51の付勢力に抗しつつこの筒状部材52が、図6に示すように、後退位置に後退した場合にのみ遮蔽部材55が((矢印Z2方向に)移動してレーザ照射口23が開放し、レーザ光が皮膚面Sに照射される。一方、筒状部材52の先端部を皮膚面Sに押圧していない場合、コイルスプリング51の付勢力によって筒状部材52が前進位置に定位し(とどまり)、遮蔽部材55も移動しないことになるから、レーザ照射口23の閉塞状態が維持され皮膚面Sへのレーザ光の照射が阻止される。したがって、トリートメント装置1によれば、トリートメントを行うべき皮膚面Sとレーザ光のレーザ照射口23とが所定の距離内に近接してはじめてレーザ光が照射可能となるので、意図しないレーザ光の照射を防止することができる。また、トリートメント装置1では、筒状部材52の後退動作と、各接触子25a、25b、25cの皮膚面Sへの接触動作との二つの動作が共に行われてはじめてレーザ光が照射される二重のプロテクト機能を備えているので、トリートメントを行う際の安全性をより高めることができる。

[0041] ここで、各接触子25a、25b、25cは、図2、図4及び図5に示すように、トリートメント対象の皮膚面とレーザ照射口23とを確実に対向させた状態で、レーザ光の照射を開始させるための好ましいレイアウトで配置されている。すなわち、これらの接触子25a、25b、25cは、レーザ照射口23のほぼ外周縁上に設けられ、且つこの外周縁を周回する方向にほぼ等しい間隔を空けてそれぞれ配置されている。詳細には、円形状に穿孔されたレーザ照射口23の外周縁を内接させ得る正三角形の三つの頂点部分に各接触子25a、25b、25cがそれぞれ配置されている。

[0042] タッチセンサ回路28は、図7及び図8に示すように、各接触子25a、25b、25cが皮膚に接触したときに発生する微弱な交流電圧を、それぞれ帯域フィルタ33、整流回路34、増幅器35を介して直流電圧に変換し、これを波形整形、レベル調整、オフセット調整した後、A/D変換器36、インタフェース32を介してCPU31に入力するように構成されている。なお、タッチセンサ回路28は、接点式その他、静電容量や抵抗などのインピーダンス変化を検知するものや、圧電素子によって圧力変化を検知するものでもよい。

[0043] タッチセンサ回路28は、以上のような構成で、各接触子25a、25b、25cの電圧値を読み込んで所定の交流電圧が発生しているか否かを判定し、各接触子25a、25b

、25cの両方に所定の交流電圧が発生しているとき、レーザダイオード20のレーザ駆動回路30にオン信号を出力する。すなわち、レーザ照射装置5は、各接触子25a、25b、25cを全て皮膚面に接触させてはじめてレーザ光が照射されるように構成されている。これにより、意図しない生体部分に誤ってレーザ光が照射されてしまうおそれがなく装置の安全性が高められている。このようなタッチセンサ回路28は、レーザ照射装置5に内蔵された例えば前記制御チップ16によって実現されている。

[0044] このように、本実施形態に係るトリートメント装置1によれば、筒状部材52の先端部を皮膚面Sに押圧し筒状部材52を後退させることより連動する遮蔽部材(シャッタ)55の開放動作と、各接触子25a、25b、25cの皮膚面Sへの接触動作と、の二つの動作が共に行われてはじめてレーザ光が照射されるので、レーザ光の誤った照射を防止する二重のプロテクト機能を実質的に備えていることになり、これにより、トリートメントを行う際の安全性をより高めることができる。

[0045] また、レーザ照射装置5が備えるレーザダイオード20は、発光部断面積が、数 $\mu\text{m}$ 〜数十 $\mu\text{m}$ オーダの非常に小さい面積となるので、He-Neレーザなどのように高指向性を持つ平行な細い直線ビームにはならず、 $30^\circ$ 〜 $45^\circ$ の角度で放射状に広がりつつ出射される。すなわち、レーザ照射装置5では、レーザ光を集光する集光レンズなどを用いていないため、レーザの焦点位置が存在せず、安全性に対する配慮がなされている。

[0046] 以上、本発明を実施の形態により具体的に説明したが、本発明はこの実施形態にのみ限定されるものではなく、その要旨を逸脱しない範囲で種々変更可能である。例えば、トリートメント装置1のヘッド部22にCCD(Charge Coupled Device)などを搭載させるとともに、このCCDによって撮像された皮膚面上の被照射部分やその周辺部分の画像を表示させる液晶ディスプレイなどをレーザ照射装置5の筐体部分などに設けてもよい。

[0047] また、図9に示すように、レーザダイオード20から放出されたレーザ光を集光する光学系として凸レンズ24aを付加してもよい。このような凸レンズ24aを付加する場合、この凸レンズ24aにより集光されるレーザ光の焦点位置R2が、各接触子25a、25b、25cにおける皮膚面Sとの接触部位の位置R1よりも、レーザダイオード20側(矢印Z2

方向側)になるように、これら接触子、凸レンズ及びレーザダイオードのレイアウトを考慮して、それぞれを設置することが望ましい。図9に示すレイアウトを適用することで、レーザ光の焦点位置R2が、皮膚面S上に重なるおそれがなく、さらに言えば、皮膚面S上には焦点位置R2を越えて、再び分散されるエネルギー密度の低下したレーザ光が照射されることになり、トリートメントを行う際の安全性が確保される。

[0048] また、図10に示すように、コイルスプリング51の付勢力に抗しつつ筒状部材52が、矢印Z2方向に後退し、当該筒状部材52が後退位置まで移動したことを検出する検出スイッチ56を設けてもよい。この検出スイッチ56としては、後退位置まで移動した筒状部材52の例えば後端部と接触する位置に配置されたプッシュスイッチなどが例示される。さらに、この場合、検出スイッチ56により筒状部材52の後退位置への移動が検出されない状態において、レーザ光照射機構を構成する例えばレーザダイオード20の駆動を阻止する光照射阻止手段としてCPU31及びレーザ駆動回路30(図7参照)を機能させるようにしてもよい。また、この検出スイッチ56による検出結果、つまり筒状部材52が後退位置まで後退したか否かに応じて、遮蔽部材55aを移動制御する機構を追加し、これにより、レーザ照射口23の開閉を制御するようにしてもよい。このような形態で検出スイッチ56を用いることで、ユーザが意図しないレーザ光の照射をより確実に防止することができる。

[0049] さらに、図4などに示した円筒型のヘッド部22に代えて、図11の斜視図及び図12の平面図に示すように、上記筒状部材52と同様の機能を有する角型の管状部材62、台座64などからなる断面矩形(長方形)の管状のヘッド部61を適用してもよい。このヘッド部61には、例えば矩形状の穴(角型の長穴)がレーザ照射口63として設けられている。また、ヘッド部61には、レーザ照射口63を周縁から囲うように、タッチセンサ機能を実現させる少なくとも三つ以上の接触子65a、65b、65cが配置されている。

[0050] ここで、ヘッド部61の内部の構造について、図11及び図12に加え、図13に基づきその説明を行う。なお、図13は、ヘッド部61に内蔵された光学系を模式的に示す斜視図である。

[0051] すなわち、ヘッド部61に内蔵されるレーザダイオード20とヘッド部61の先端のレー

ザ照射口63との間(レーザダイオード20から放出されるレーザ光の光路上)には、縦横比の異なるレーザスポットQを皮膚面S上に形成するための樽型形状のレンズ24bが配置されている。このレンズ24bにおけるレーザ光の入射面及び出射面の形状は、縦横の曲率が異なるように膨出させて形成されている。詳細には、図13において、矢印Y1-Y2方向に沿って起立した姿勢で図示されるレンズ24bは、レーザ光の入射部分及び出射部分の水平断面の曲率が、その垂直断面の曲率よりも大きくなるように形成されている。すなわち、レンズ24bは、レーザダイオード20側から入射したレーザ光の断面形状の縦横比を変化させつつ当該レーザ光をレーザ照射口63側に射出する。

[0052] また、上記したレーザ照射口63は、レンズ24bを通過したレーザ光の断面形状の縦横比に対応させた形状(レーザ光を遮ることなく、その全ての光束を通過させることのできる形状及びサイズを有する長細い矩形穴)で形成されている。すなわち、レーザ光がレンズ24b及びレーザ照射口63を通過して皮膚面S上に形成するレーザスポットQは、図11～図13に示すように、レーザ照射口63の長手方向(矢印Y1-Y2方向)が長軸となり、一方、レーザ照射口63の短手方向(矢印X1-X2方向)が短軸となる長細い照射スポットになる。

[0053] したがって、皮膚面S上に形成されるレーザスポットQの短軸方向(矢印X1-X2方向)に、ヘッド部61をユーザが移動させることで、皮膚面Sに対するトリートメント(レーザ光の照射による熱的作用の付与)を効率的に行うことができる。また、長細いレーザスポットを形成するためのレンズ24bを配置することに代えて、例えば、複数のレーザダイオードを配置するようにしてもよい。この場合、複数のレーザダイオードは、レーザ照射口63と対向する位置に設けられ、且つこのレーザ照射口63の長手方向に沿った方向に並べて配置されることが望ましい。さらに、図11、図12などに示したヘッド部61に代えて、図14の斜視図及び図15の平面図に示すように、断面がほぼ正方形の管状部材72及び台座74、並びに、矩形状のレーザ照射口73、樽型形状のレンズ24c、及び接触子75a、75b、75cを備えるヘッド部71を適用してトリートメント装置を構成してもよい。このヘッド部71によっても、上記したヘッド部61とほぼ同様の効果を期待できる。



### 産業上の利用可能性

[0054] 本発明は、電子・電機機器製造業などにおいて広く利用することができる。

## 請求の範囲

- [1] トリートメント対象の皮膚面に向けて照射口より光を照射する光照射機構と、  
前記皮膚面と前記照射口との離間距離に基づいて前記照射口を開閉する照射口  
開閉機構と、  
を具備することを特徴とするトリートメント装置。
- [2] 前記照射口開閉機構が、  
前記照射口を周縁から包囲するとともに、先端部が前記照射口から突出する前進  
位置と前記前進位置から後退する所定の後退位置との間を進退移動自在に設けら  
れた筒状部材と、  
前記筒状部材の進退移動に連動し前記筒状部材が前記前進位置に移動した場合  
に前記照射口を閉塞し、前記筒状部材が前記後退位置に移動した場合に前記照射  
口を開放する遮蔽部材と、  
前記筒状部材を前記前進位置に付勢する付勢部材と、  
を具備することを特徴とする請求項1記載のトリートメント装置。
- [3] 前記筒状部材の内側から前記照射口の周縁を包囲するように配置された少なくとも  
三つ以上の接触子と、  
前記皮膚面に対する全ての前記接触子の接触を検出して前記光照射機構を作動  
させるタッチセンサ機構と、  
をさらに具備することを特徴とする請求項2記載のトリートメント装置。
- [4] 前記光照射機構によって照射される光は、レーザ光であることを特徴とする請求項  
2記載のトリートメント装置。
- [5] 前記光照射機構が、  
光源と、  
前記光源から放出された光を集光する光学系とを備え、  
さらに、前記光学系により集光される光の焦点位置が、前記接触子における前記皮  
膚面との接触部分の位置よりも、前記光源側にあることを特徴とする請求項3記載の  
トリートメント装置。
- [6] 前記筒状部材が前記後退位置に移動したことを検出する検出手段と、

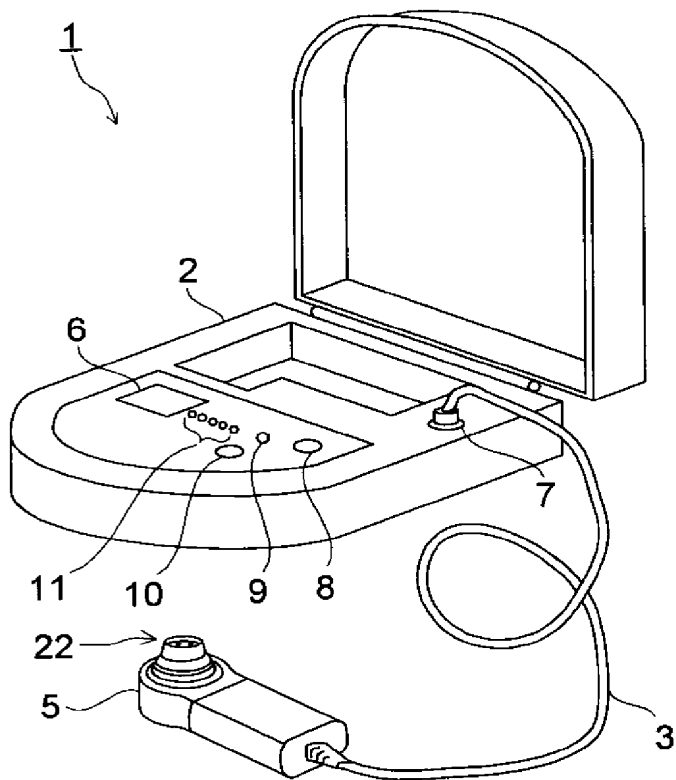
前記検出手段により前記筒状部材の前記後退位置への移動が検出されない状態では、前記光照射機構の駆動を阻止する光照射阻止手段と、  
を具備することを特徴とする請求項2記載のトリートメント装置。

[7] 前記光源から放出された光を入射しこの入射した光の断面形状の縦横比を変化させつつ当該光を出射するレンズを備えることを特徴とする請求項1記載のトリートメント装置。

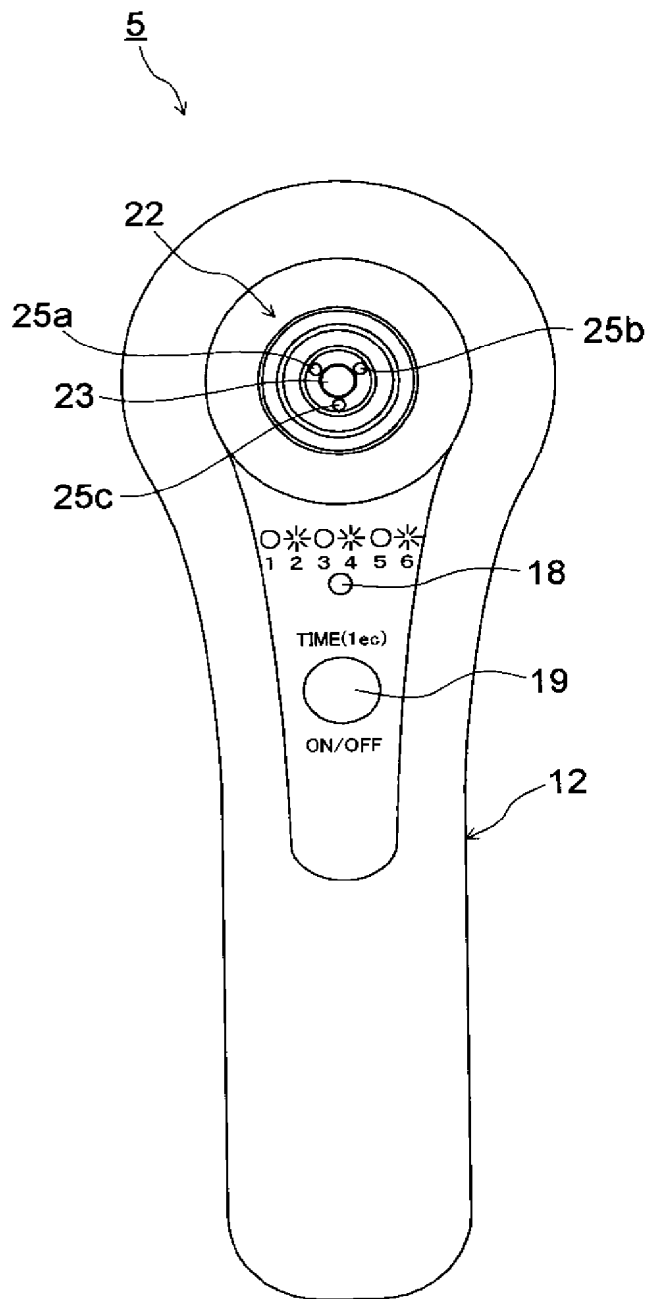
[8] 前記レーザ照射口は、前記レンズを通過した光の断面形状の縦横比に対応させた矩形状の穴により形成されていることを特徴とする請求項7記載のトリートメント装置。

[9] 前記レンズにおける光の入射面及び出射面となる部位は、縦横の曲率が異なるように膨出させた形状で形成されていることを特徴とする請求項7記載のトリートメント装置。

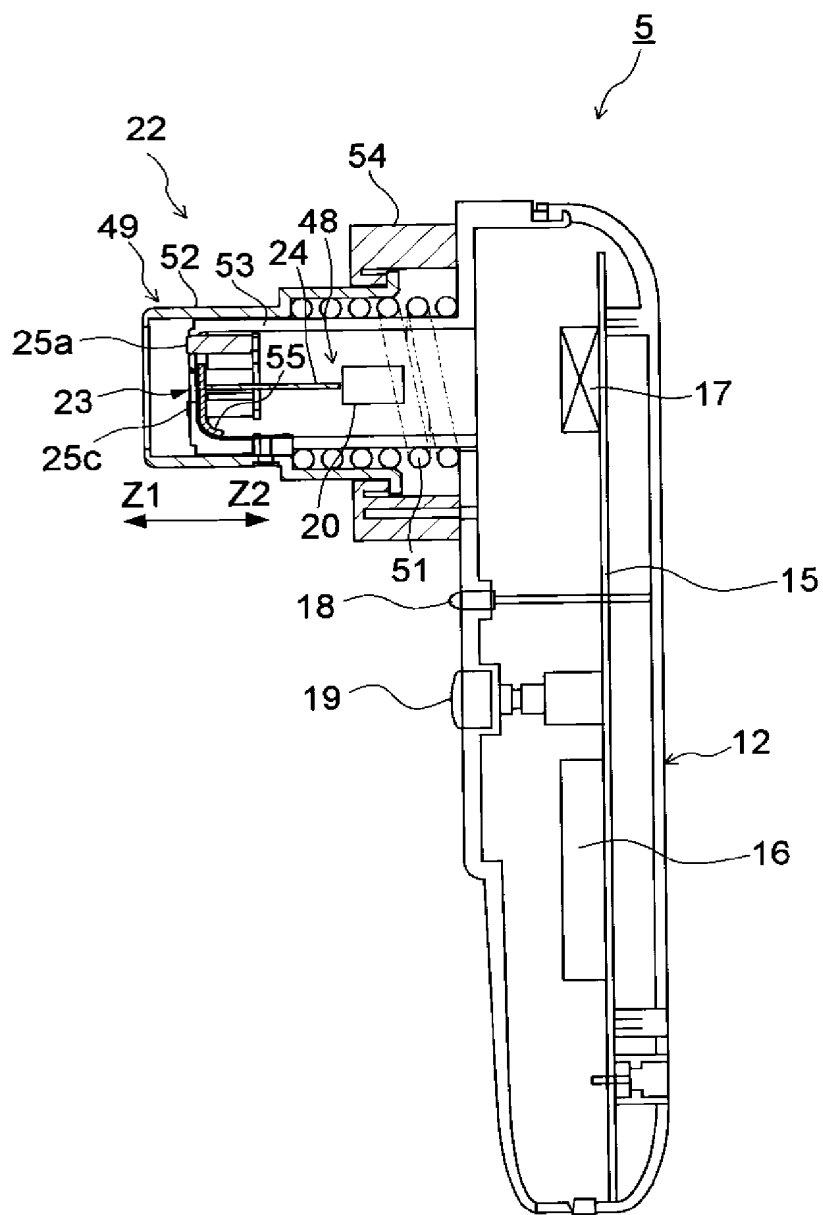
[[図1]]



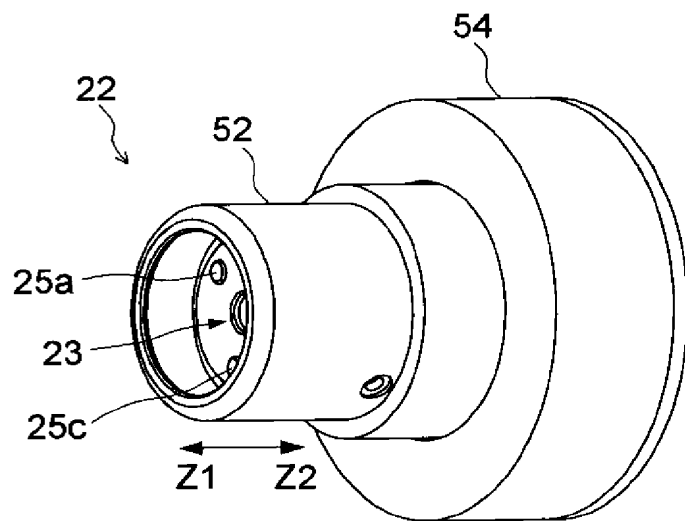
[図2]



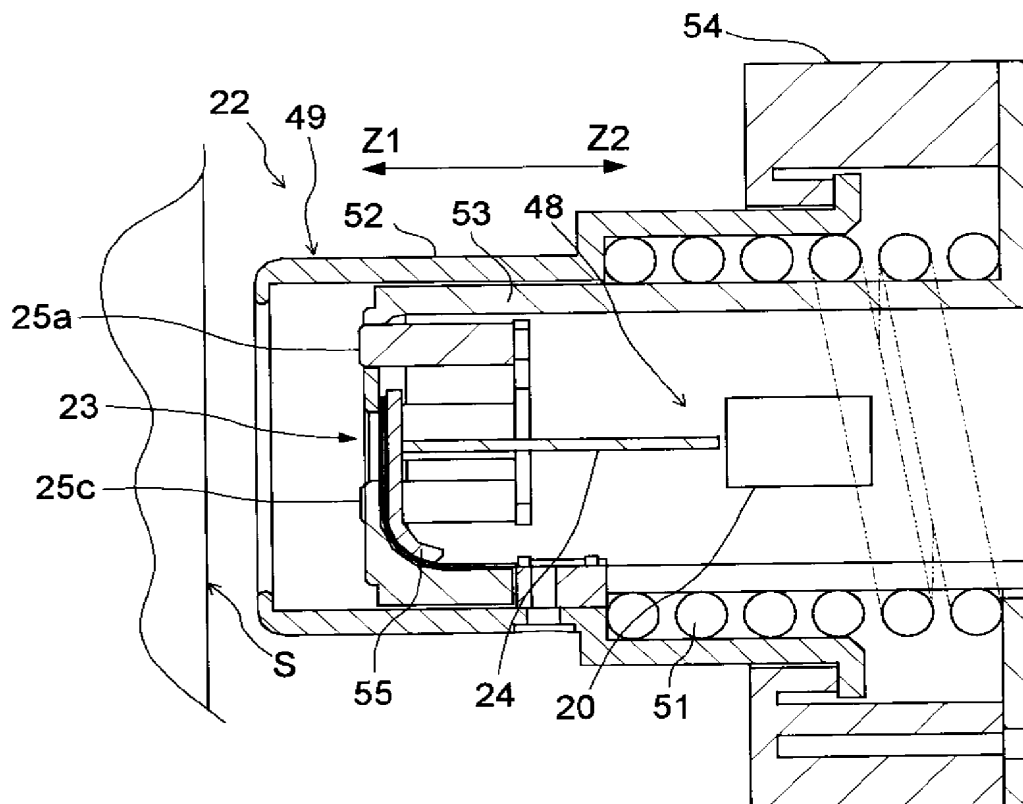
[図3]



[図4]



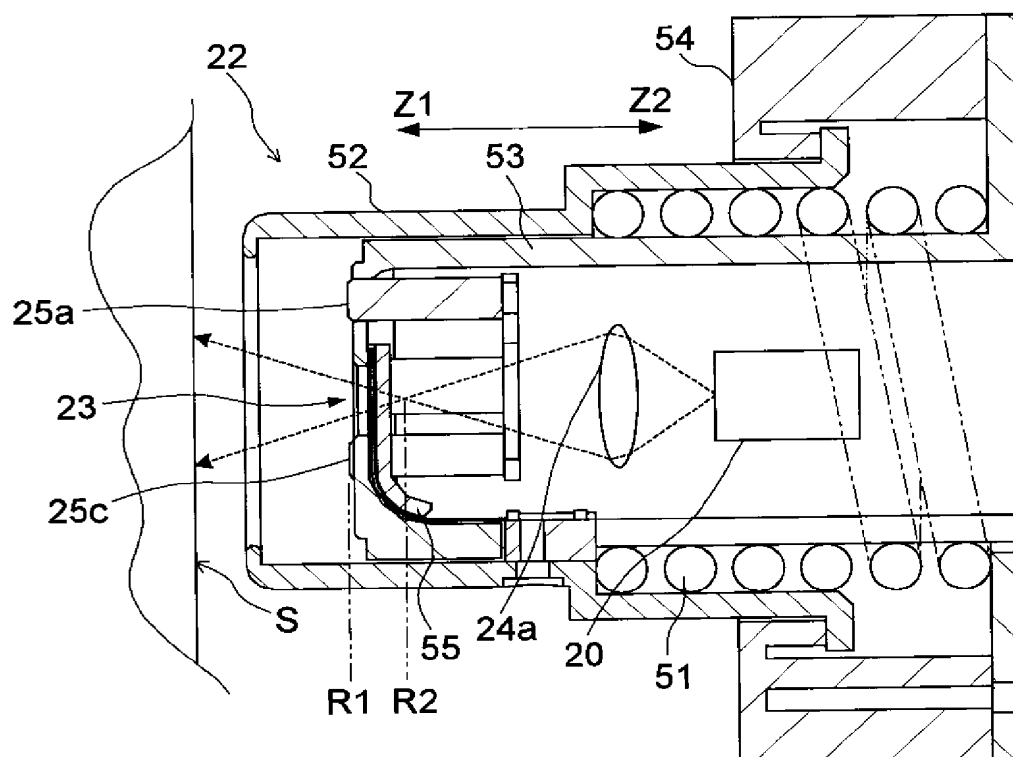
[図5]



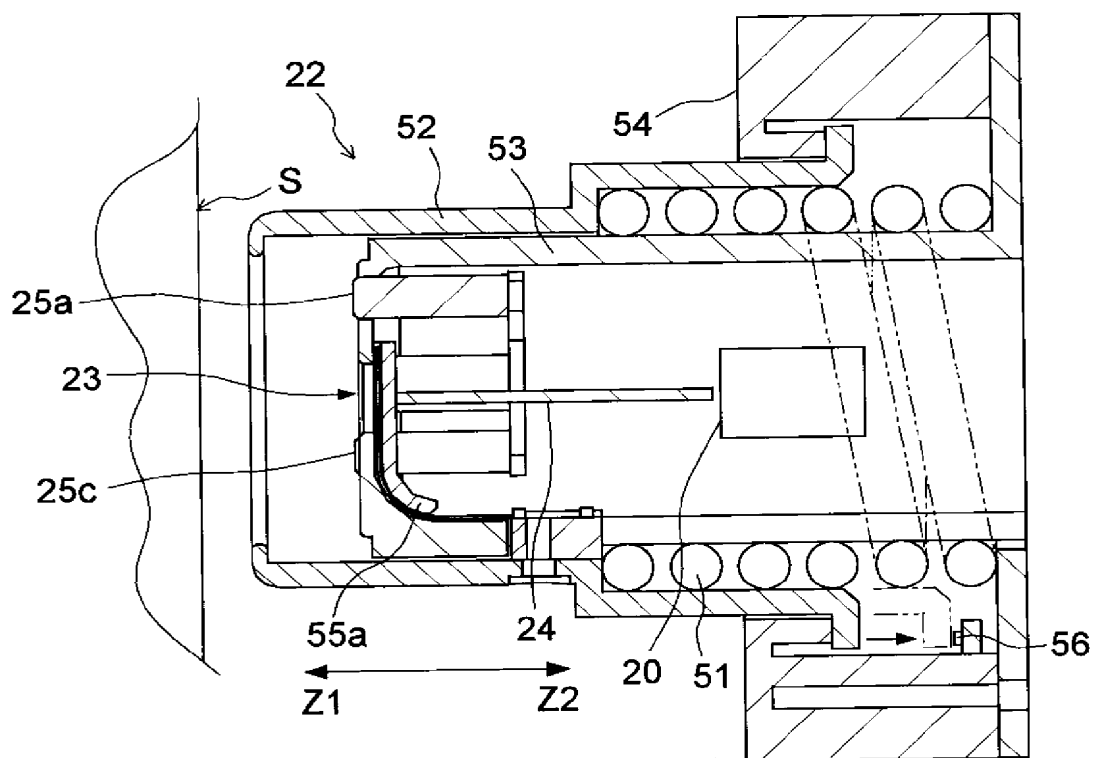




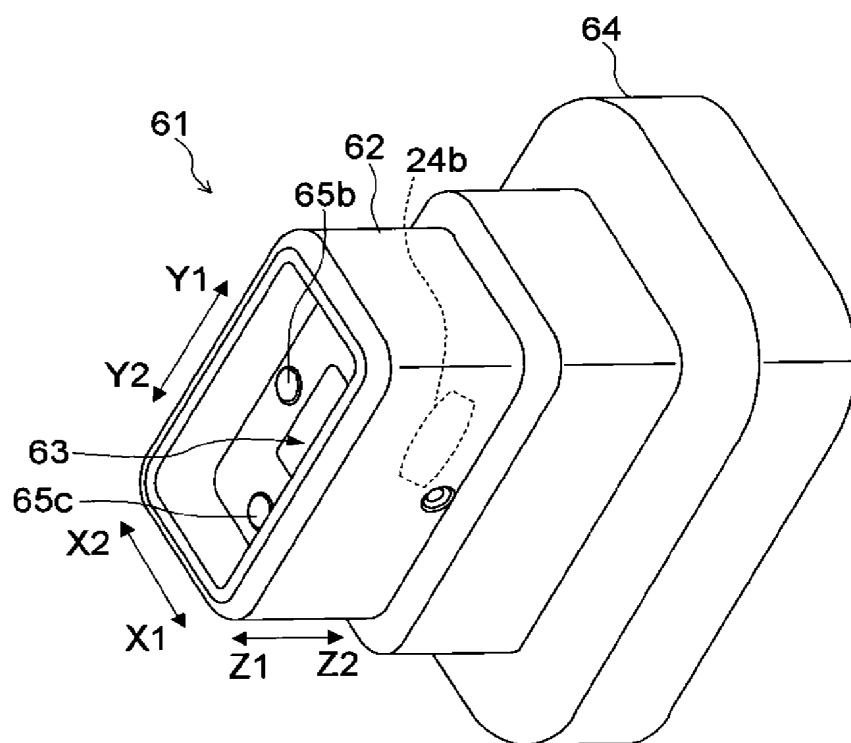
[[図9]]



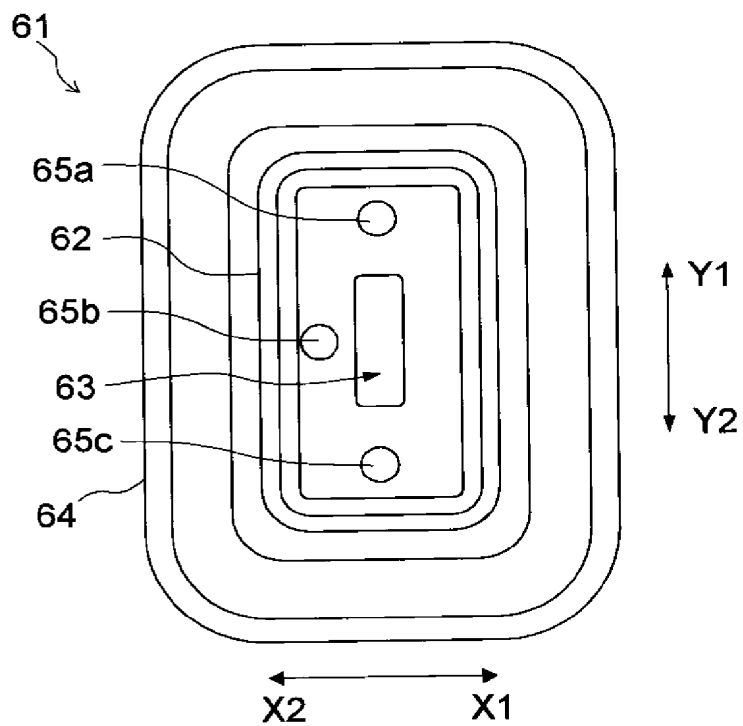
[[図10]]



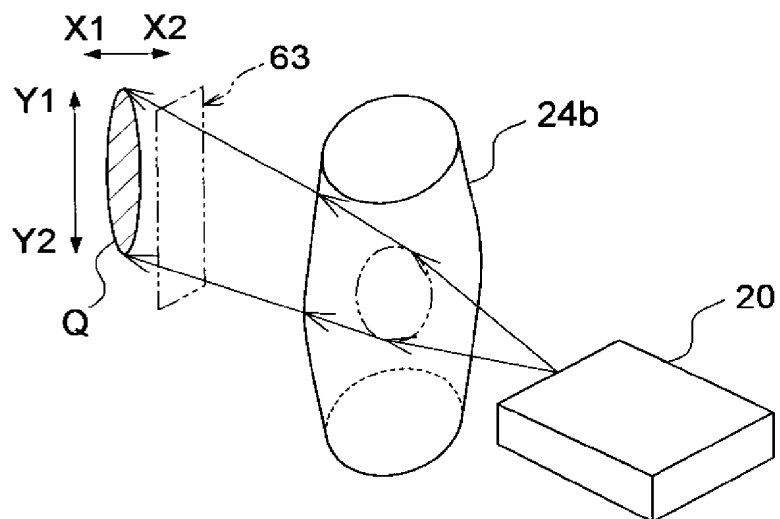
[[図11]]



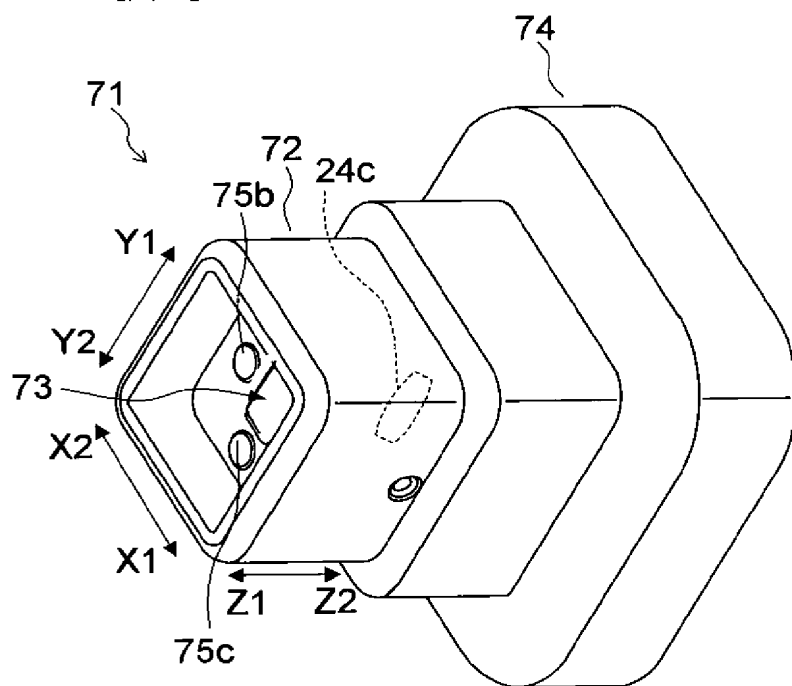
[[図12]]



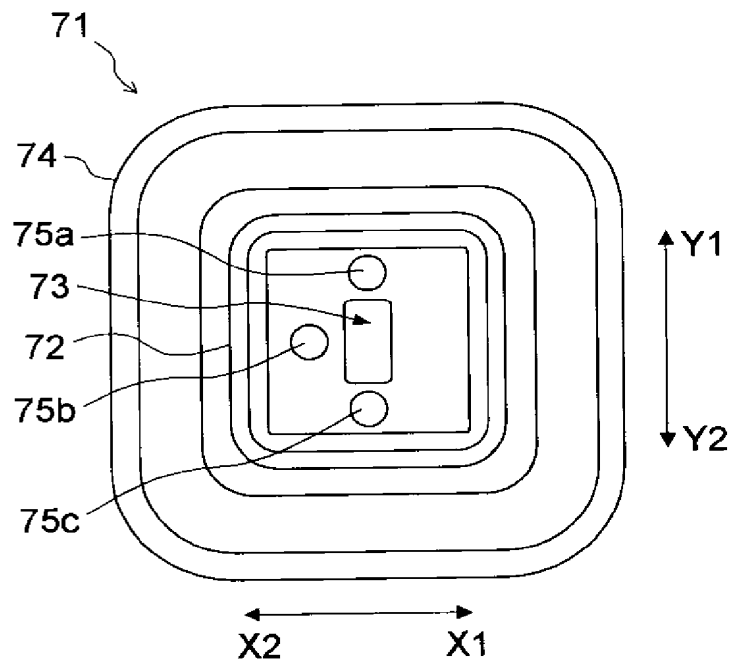
[[図13]]



[[図14]]



[図15]



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2005/005282

A. CLASSIFICATION OF SUBJECT MATTER  
Int.Cl<sup>7</sup> A61N5/06, A45D26/00, A61B18/20

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl<sup>7</sup> A61N5/06, A45D26/00, A61B18/20

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

|                           |           |                            |           |
|---------------------------|-----------|----------------------------|-----------|
| Jitsuyo Shinan Koho       | 1922-1996 | Jitsuyo Shinan Toroku Koho | 1996-2005 |
| Kokai Jitsuyo Shinan Koho | 1971-2005 | Toroku Jitsuyo Shinan Koho | 1994-2005 |

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| Y         | JP 60-63068 A (Fuji Photo Optical Co., Ltd.),<br>11 April, 1985 (11.04.85),<br>Full text; all drawings<br>(Family: none)    | 1-9                   |
| Y         | JP 2002-355320 A (YAMAN Ltd.),<br>10 December, 2002 (10.12.02),<br>Par. Nos. [0027] to [0030]; Figs. 2, 3<br>(Family: none) | 1-9                   |
| Y         | JP 2002-306230 A (YAMAN Ltd.),<br>22 October, 2002 (22.10.02),<br>Par. Nos. [0021] to [0027]; Fig. 6<br>(Family: none)      | 5                     |



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search  
02 June, 2005 (02.06.05)

Date of mailing of the international search report  
21 June, 2005 (21.06.05)

Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2005/005282

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| Y         | JP 59-228862 A (Fuji Photo Optical Co., Ltd.),<br>22 December, 1984 (22.12.84),<br>Page 4, upper right column, line 15 to lower<br>left column, line 20; Fig. 2<br>(Family: none) | 6                     |
| Y         | JP 2000-334052 A (YAMAN Ltd.),<br>05 December, 2000 (05.12.00),<br>Par. Nos. [0010] to [0011]; Figs. 2 to 4<br>(Family: none)   | 7-9                   |

|   |  |  |  |
|---|--|--|--|
| A. 発明の属する分野の分類 (国際特許分類 (IPC))<br>Int.Cl.7 A61N5/06, A45D26/00, A61B18/20  |  |  |  |
| B. 調査を行った分野<br>調査を行った最小限資料 (国際特許分類 (IPC))<br>Int.Cl.7 A61N5/06, A45D26/00, A61B18/20  |  |  |  |
| 最小限資料以外の資料で調査を行った分野に含まれるもの<br>日本国実用新案公報 1922-1996年<br>日本国公開実用新案公報 1971-2005年<br>日本国実用新案登録公報 1996-2005年<br>日本国登録実用新案公報 1994-2005年  |  |  |  |
| 国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)   |  |  |  |
| C. 関連すると認められる文献   |  |  |  |
| 引用文献の<br>カテゴリー*   | 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示  | 関連する<br>請求の範囲の番号                                       |  |
| Y   | JP 60-63068 A (富士写真光機株式会社) 1985. 04. 11, 全文、全図 (ファミリーなし)                       | 1-9  |  |
| Y   | JP 2002-355320 A (ヤーマン株式会社) 2002. 12. 10, 段落【0027】 - 【0030】、第 2, 3 図 (ファミリーなし) | 1-9  |  |
| Y   | JP 2002-306230 A (ヤーマン株式会社) 2002. 10. 22, 段落【0021】 - 【0027】、第 6 図 (ファミリーなし)    | 5  |  |
| <input checked="" type="checkbox"/> C欄の続きにも文献が列挙されている。 <input type="checkbox"/> パテントファミリーに関する別紙を参照。   |  |  |  |
| * 引用文献のカテゴリー<br>「A」特に関連のある文献ではなく、一般的技術水準を示すもの<br>「E」国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの<br>「L」優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す)<br>「O」口頭による開示、使用、展示等に言及する文献<br>「P」国際出願日前で、かつ優先権の主張の基礎となる出願日の後に公表された文献<br>「T」国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの<br>「X」特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの<br>「Y」特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの<br>「&」同一パテントファミリー文献 |  |  |  |
| 国際調査を完了した日<br>02. 06. 2005  |  | 国際調査報告の発送日<br>21. 6. 2005                              |  |
| 国際調査機関の名称及びあて先<br>日本国特許庁 (ISA/J P)<br>郵便番号100-8915<br>東京都千代田区霞が関三丁目4番3号   |  | 特許庁審査官 (権限のある職員)<br>西山 智宏<br>電話番号 03-3581-1101 内線 3346 |  |

| C (続き). 関連すると認められる文献 |  |                  |
|----------------------|--|------------------|
| 引用文献の<br>カテゴリー*      | 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示  | 関連する<br>請求の範囲の番号 |
| Y                    | JP 59-228862 A (富士写真光機株式会社) 1984.12.22, 第4頁右上<br>欄第15行-左下欄第20行、第2図 (ファミリーなし) | 6                |
| Y                    | JP 2000-334052 A (ヤーマン株式会社) 2000.12.05, 段落【0010】 -<br>【0011】、第2-4図 (ファミリーなし) | 7-9              |



(19) World Intellectual Property  
Organization  
International Bureau



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20 October 2005 (20.10.2005)

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(30) Priority Data:  
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(71) Applicant (for all designated States except US): **THE GENERAL HOSPITAL CORPORATION** [US/US]; 55 Fruit Street, Boston, MA 02114 (US).

(72) Inventors: **MANSTEIN, Dieter**; 4 Longfellow Place, Apt. 2005, Boston, MA 02114 (US). **ANDERSON, R., Rox**; 399 Marrett Road, Lexington, MA 02173 (US).

(74) Agents: **KOWALSKI, Thomas, J.** et al.; Frommer Lawrence & Haug LLP, 745 Fifth Avenue, New York, NY 10151 (US).

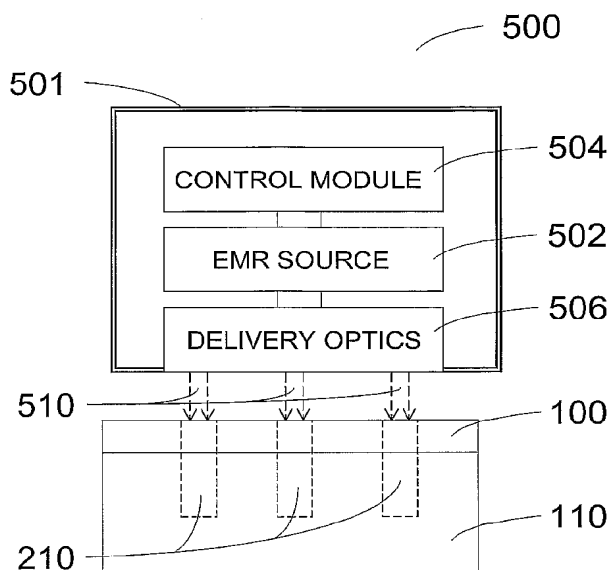
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:  
— without international search report and to be republished upon receipt of that report

[Continued on next page]

(54) Title: METHOD AND APPARATUS FOR DERMATOLOGICAL TREATMENT



(57) Abstract: The present invention provides improved methods and apparatus for skin treatment. The apparatus includes multiple sources of optical energy or several blades that are scanned along a region of skin to form micro-line patterns of damaged tissue. The micro-lines are small in at least one dimension, having a width of less than about 1 mm, and the wounded regions promote beneficial results by stimulation of wound healing and tissue remodeling.

WO 2005/096981 A2



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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

TITLE OF THE INVENTION

## METHOD AND APPARATUS FOR DERMATOLOGICAL TREATMENT

RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application Serial No.  
5 60/558,397, filed on April 1, 2004, and to U.S. Provisional Application Serial No.  
60/558,476, filed on April 1, 2004.

INCORPORATION BY REFERENCE

The foregoing applications, and all documents cited therein or during their  
prosecution (“appln cited documents”) and all documents cited or referenced in the appln  
10 cited documents, and all documents cited or referenced herein (“herein cited documents”),  
and all documents cited or referenced in herein cited documents, together with any  
manufacturer’s instructions, descriptions, product specifications, and product sheets for any  
products mentioned herein or in any document incorporated by reference herein, are hereby  
incorporated herein by reference, and may be employed in the practice of the invention.

15 FIELD OF THE INVENTION

The present invention is directed to an improved method for skin treatment. More  
specifically, it is directed to a method termed “fractional resurfacing” that uses  
electromagnetic radiation produced by one or more individual point sources or mechanical  
means to damage selected regions of the skin and thereby promote beneficial results by  
20 stimulation of wound healing and tissue remodeling.

BACKGROUND OF THE INVENTION

Skin is primarily made of two layers. The outer layer, or epidermis, has a depth of  
approximately 100  $\mu\text{m}$ . The inner layer, or dermis, has depth of approximately 3000  $\mu\text{m}$  from  
the outer surface of the skin. In the present disclosure, ‘dermal tissue’ refers to both the dermis  
25 and the epidermis. The term ‘dermal tissue’ is also used interchangeably with the term ‘skin’  
herein.

There is ongoing demand for procedures to improve skin defects. Such improvements  
may involve, but are not limited to, reducing wrinkles or reducing dyschromia (any  
abnormality or irregularity of skin color resulting either from irregular pigment distribution or  
30 dilatated blood vessels). Various techniques providing this objective have been introduced in  
recent years. The different techniques can be generally categorized into two groups of  
treatment modalities: ablative laser skin resurfacing (“LSR”) and non-ablative collagen  
remodeling (“NCR”). The first group of treatment modalities, LSR, includes causing fairly

extensive thermal damage to the epidermis and/or dermis, while the second group, NCR, is designed to avoid thermal damage of the epidermis.

LSR is considered to be an effective laser treatment for repairing skin. In a typical LSR procedure, shown schematically in Fig. 1, a region of the epidermis 100 and a corresponding region of the dermis 110 beneath it are thermally damaged to promote wound healing. Electromagnetic energy 120 is directed towards a region of skin, ablating the skin and removing both epidermal and dermal tissue in region 130. LSR with pulsed CO<sub>2</sub> or Er:YAG lasers, which may be referred to in the art as laser resurfacing or ablative resurfacing, is considered to be an effective treatment option for signs of photo aged skin, chronically aged skin, scars, superficial pigmented lesions, stretch marks, and superficial skin lesions. However, patients may experience major drawbacks after each LSR treatment, including edema, oozing, and burning discomfort during first fourteen (14) days after treatment. These major drawbacks can be unacceptable for many patients. A further problem with LSR procedures is that the procedures are relatively painful and therefore generally require an application of a significant amount of analgesia. While LSR of relatively small areas can be performed under local anesthesia provided by injection of an anestheticum, LSR of relatively large areas is frequently performed under general anesthesia or after nerve blockade by multiple injections of anesthetic.

A limitation of LSR using CO<sub>2</sub> or Er:YAG lasers is that ablative laser resurfacing generally can not be performed on the patients with dark complexions. The removal of pigmented epidermis tissue can cause severe cosmetic disfigurement to patients with a dark complexion, which may last from several weeks up to years, which is considered by most patients and physicians to be unacceptable. Another limitation of LSR is that ablative resurfacing in areas other than the face generally have a greater risk of scarring. LSR procedures in areas other than the face result in an increased incidence of an unacceptable scar formation because the recovery from skin injury within these areas is not very effective.

In an attempt to overcome the problems associated with LSR procedures, a group of NCR techniques has emerged. These techniques are variously referred to in the art as non-ablative resurfacing, non-ablative subsurfacing, or non-ablative skin remodeling. NCR techniques generally utilize non-ablative lasers, flashlamps, or radio frequency current to damage dermal tissue while sparing damage to the epidermal tissue. The concept behind NCR techniques is that the thermal damage of only the dermal tissues is thought to induce wound healing which results in a biological repair and a formation of new dermal collagen. This type of wound healing can result in a decrease of photoaging related structural damage.

Avoiding epidermal damage in NCR techniques decreases the severity and duration of treatment related side effects. In particular, post procedural oozing, crusting, pigmentary changes and incidence of infections due to prolonged loss of the epidermal barrier function can usually be avoided by using the NCR techniques.

In the NCR method of skin treatment, illustrated schematically in Fig. 2, selective portions of dermal tissue 135 within the dermal layer 110 are heated to induce wound healing without damaging the epidermis 100 above. Selective dermal damage that leaves the epidermis undamaged can be achieved by cooling the surface of the skin and focusing electromagnetic energy 120, which may be a laser beam, onto dermal region 135 using lens 125. Other strategies are also applied using nonablative lasers to achieve damage to the dermis while sparing the epidermis in NCR treatment methods. Nonablative lasers used in NCR procedures generally have a deeper dermal penetration depth as compared to ablative lasers used in LSR procedures. Wavelengths in the near infrared spectrum can be used. These wavelengths cause the non-ablative laser to have a deeper penetration depth than the very superficially-absorbed ablative Er: YAG and CO<sub>2</sub> lasers. Examples of NCR techniques and apparatus are disclosed by Anderson et al. in U.S. Patent Publication No. 2002/0161357.

While it has been demonstrated that these NCR techniques can assist in avoiding epidermal damage, one of the major drawbacks of these techniques is their limited efficacies. The improvement of photoaged skin or scars after the treatment with NCR techniques is significantly smaller than the improvements found when LSR ablative techniques are utilized. Even after multiple treatments, the clinical improvement is often far below the patient's expectations. In addition, clinical improvement is usually several months delayed after a series of treatment procedures. NCR is moderately effective for wrinkle removal and is generally not effective for dyschromia. One advantage of NCR is that it does not have the undesirable side effects that are characteristic of the LSR treatment, such as the risk of scarring or infection.

Another limitation of NCR procedures relates to the breadth of acceptable treatment parameters for safe and effective treatment of dermatological disorders. The NCR procedures generally rely on an optimum coordination of laser energy and cooling parameters, which can result in an unwanted temperature profile within the skin leading to either no therapeutic effect or scar formation due to the overheating of a relatively large volume of the tissue.

A further problem of both ablative and nonablative resurfacing is that the role of keratinocytes in the wound healing response is not capitalized upon. Keratinocyte plays an

active role in the wound healing response by releasing cytokines when the keratinocyte is damaged. During traditional ablative resurfacing procedures, the keratinocytes are removed from the skin along with the epidermis, thereby removing them from the healing process altogether. On the other hand, in traditional non-ablative procedures, the keratinocytes, which are located in the epidermis, are not damaged, and therefore do not release cytokines to aid in the healing process.

Citation or identification of any document in this application is not an admission that such document is available as prior art to the present invention.

### SUMMARY OF THE INVENTION

In view of the above-mentioned disadvantages and limitations of LSR and NCR, there is an increasing demand for an effective and safe treatment that repairs or alleviates skin defects. In recognition of this demand, the present invention relates to improved methods and apparatus for treating skin. Methods and apparatus according to the present invention are safe, effective, and the various embodiments of the apparatus are relatively simple to manufacture and use.

In an embodiment according to the present invention, methods and apparatus for damaging dermal tissue in particular patterns ('micro-lines') to promote effective and fast wound healing are described. 'Damaging' is defined as inducing cell death in one or more regions of the dermal tissue of interest ('lethal damage'), or stimulating the release of cytokines, heat shock proteins, and other wound healing factors without stimulating necrotic cell death ('sublethal damage'). 'Micro-lines' are narrow regions of damaged dermal tissue, generally less than 1 mm in width, that extend from the surface of the skin into the epidermis and, optionally, through the epidermis and into the dermal layer. The micro-lines are long in one direction along the surface of the skin, generally at least four to five times as long as the width of the micro-lines, and may traverse part or all of the region of skin being treated.

In another embodiment according to the present invention, a method for damaging dermal tissue is provided wherein a plurality of micro-lines of damaged regions are created that extend from the skin surface into the epidermal tissue and, optionally, into the dermal tissue.

In another embodiment of this invention, several micro-lines of damaged regions of dermal tissue may be formed simultaneously. The micro-lines thus formed may be nearly parallel, and may be linear, curved, or wavy.

In another embodiment according to the present invention, the fractional coverage of the skin surface with micro-lines of damaged tissue in the region of skin being treated is

preferably about 50%. In other embodiments according to the present invention, the fractional coverage of the skin by micro-lines can range from about 10% to about 80%. The fractional coverage can be controlled by varying the width of the individual micro-lines, by varying the spacing between adjacent micro-lines, or by varying both the width and spacing of the micro-lines. The fractional coverage may also be increased by creating more than one set of micro-lines over a given region of skin being treated.

In yet another embodiment according to the present invention, one or more sources of electromagnetic radiation ('EMR') such as a laser may be used to create the plurality of micro-lines.

In yet another embodiment according to the present invention, one or more diamond knives or scalpels or other mechanical implements may create the plurality of micro-lines.

In another embodiment of the invention, an apparatus for treating skin by creating micro-lines of damage is provided. The apparatus includes a damaging means for causing cell death in dermal tissue, and an optional control unit for controlling the damaging means, which may be used to create a plurality of micro-lines in the dermal tissue of interest.

In yet another embodiment according to the present invention, the apparatus comprises one or more optical energy sources such as a laser as damaging means to create the plurality of micro-lines.

In yet another embodiment according to the present invention, the apparatus comprises one or more diamond knives or scalpels or other mechanical implements as damaging means to create the plurality of micro-lines.

In yet another embodiment according to the present invention, the apparatus comprises a radio frequency (RF) device as damaging means to create the plurality of micro-lines.

In another embodiment of the invention, the apparatus comprises a housing containing the damaging means that is manually translated across a region of the skin to produce the micro-lines.

In another embodiment of the invention, the apparatus comprises a housing containing the damaging means and a scanning mechanism that automatically translates the damaging means across a region of the skin in a controlled manner to produce the micro-lines.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The following detailed description, given by way of example, but not intended to limit the invention solely to the specific embodiments described, may best be understood in conjunction with the accompanying drawings, in which:

Fig. 1 is a schematic drawing of a cross section of a tissue treated using the LSR method.

Fig. 2 is a schematic drawing of a cross section of a tissue treated using the NCR method.

Fig. 3 is a schematic drawing of a cross section of a tissue treated in accordance with an embodiment of the present invention.

Figs. 4(a)-4(i) depict various patterns of micro-lines in accordance with an embodiment according to the present invention.

Fig. 5 is a schematic illustration of an apparatus for conducting dermatological treatments using electromagnetic energy according to one embodiment of the present invention.

Fig. 6 is a schematic illustration of an apparatus for conducting dermatological treatment using mechanical means according to one embodiment of the present invention.

Throughout the drawings, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components, or portions of the illustrated embodiments. Moreover, while the present invention will now be described in detail with reference to the Figures, it is done so in connection with the illustrative embodiments and is not limited by the particular embodiments illustrated in the Figures.

#### DETAILED DESCRIPTION OF THE INVENTION

In accordance with one embodiment of the present invention, the epidermis, the dermis, or both the epidermis and dermis may be damaged in regions that are small in at least one dimension along the surface of the skin, where 'small' denotes a size less than about one mm, to achieve the desired effects of wound healing and tissue remodeling.

In one preferred embodiment of the invention, regions of damaged tissue are created in both the dermis and epidermis for reasons that will be described below. Fig. 3 depicts a cross section of dermal tissue comprising epidermal layer 100 and dermal layer 110, treated in accordance with a present embodiment of the invention. As shown in Fig. 3, regions of damaged tissue 210 are created in the epidermis and the dermis by beams of electromagnetic energy 120. In contrast to LSR and NDR, where the purpose is to achieve homogeneous damage at a particular depth within the skin (see Figs. 1 and 2 respectively), in at least one embodiment of the present invention, the creation of micro-lines of damaged tissue extend through the epidermis but spare regions of undamaged tissue 215 surrounding each micro-line. The micro-lines of damaged tissue 210, each of which extends laterally for some distance parallel to the skin surface (corresponding to a direction into and/or out of the page for the cross-section shown in Fig. 3), together



with the regions of undamaged tissue 215 between the micro-lines, form the basis for a macroscopic treatment effect.

Methods and apparatus according to the present invention can be used, for example, to reduce the appearance of wrinkles and lines, improve skin texture, rejuvenate the appearance of the skin, reduce skin pigmentation (either generally or in specific foci such as freckles, birthmarks, lentigos or tattoos), treat dyschromia, improve the appearance of scar tissue, treat acne, and treat vascular lesions such as port-wine stains, hemangiomas, telangiectasias, venous lakes, and spider and cherry angiomas. The range of dermatological conditions that can be treated according to the present invention includes virtually any type of dermatological defect in need of correction.

The methods and apparatus according to the present invention can be used to treat skin in any patient of any age. However, the present invention is particularly useful in the treatment of aged skin, in particular photoaged skin. Likewise, the present invention can be used to treat skin anywhere on the body and is particularly well suited for the treatment of facial skin such as, for example, the perioral and periocular skin.

In one embodiment, the methods according to the present invention can be carried out without analgesia or anesthesia. However, if desired, any suitable analgesic or anesthetic methods can be used. For example, the present methods can be performed following topical administration of lidocaine. Alternatively, or additionally, the methods of the invention can be performed with conductive or convective cooling of the surface region of the skin prior to and/or during creation of the micro-lines of damaged tissue. Such cooling can be applied to reduce or eliminate perceived pain or discomfort during the treatment. Cooling can also be applied to reduce or eliminate dermal tissue damage near or at the surface of the skin, including all or part of the epidermis.

Without being bound by theory, methods of the invention are understood to induce damage or "wounding" of dermal tissue, which in turn stimulates a "wound healing response" within the dermal tissue. The wound healing response in turn promotes tissue regeneration. The term "wound" as used herein refers to physically induced tissue damage, which may or may not involve necrotic cell death. Wound healing in the skin is a process involving, among other things, the release of cytokines, heat-shock proteins, and growth factors, followed by the stimulation of cellular migration, cellular proliferation, and extracellular matrix ("ECM") remodeling. For example, it is known from corneal model systems that injured epithelial cells stimulate fibroblast myodifferentiation through one or more soluble factors, including TGF-beta. This enhances stromal remodeling. (Nakamura, K. (2003) Cornea, 2(7

Suppl):S35-47). Furthermore, stimulation of myofibroblasts, which leads to delayed tissue contraction, can produce tissue tightening. Thus, controlled myodifferentiation and myofibroblast stimulation will allow delayed and effective wound contraction and therefore, desired tightening of dermal tissue. These wound healing processes, including the remodeling of the ECM proteins collagen and elastin, are believed to contribute to the mechanism for regeneration and a rejuvenated appearance of the skin. Thus, in one embodiment, the present invention minimizes the appearance of lines and wrinkles.

The selected pattern and instrumentation used in wounding can influence the end result and the choice and combination of selected means from the options disclosed in the various embodiments of the invention disclosed herein is well within the level of skill in the art. In one embodiment, the extent of differentiation and/or contraction of myofibroblasts is modulated by the pattern of wounding and can be further enhanced by simultaneous application of applied agents. Such agents can be, for example, either topically or systemically administered. In another embodiment, further beneficial effects can result from vertical extrusion of necrotic epidermal and dermal components induced by application according to the present invention. Following thermal damage, such debris gradually migrates towards the surface of the skin before being sloughed off. Thus, controlled removal of pigment, for example melanin, can be achieved by extrusion, optionally followed by administration of an appropriate fill factor (e.g., collagen).

The present invention provides an optimal balance between the negative and positive effects of induced wounding. In one embodiment, this is achieved by damaging only a fraction of the total skin surface in the dermal tissue of interest. In particular, according to the methods of the present invention, the skin is damaged in micro-line patterns, wherein line-shaped regions of wounding that extend into the epidermis, and optionally into the dermis, are surrounded by non-wounded areas. As a result, the extent of the wound-healing response is controlled, and the aesthetically undesirable side effects of wounding, such as edema, oozing, crusting, and burning discomfort, are reduced or eliminated.

Additionally, the present invention can restrict wounding to a fraction of cells within the dermal tissue of interest, and therefore the rate of recovery and healing is not limited by the need to generate entire cell layers anew. Instead, the "spared" cells are able to migrate laterally into the wounded areas to provide functional compensation. In this way, recovery can be rapidly achieved (e.g., re-epithelization can occur in as little as 24 hours following treatment). The micro-lines of dermal tissue damage formed when practicing the present

invention have at least one dimension that is small, which allows repopulation of the damaged region from surrounding undamaged tissue over a small migration length.

The damage-producing source parameters may also be adjusted to determine the depth of the damage in the skin. For example, in one embodiment the dermal tissue damage can be induced selectively in the outer epidermis. Importantly, it has been found that using the methods according to the present invention to induce damage in the most superficial layers of the epidermis (including the outermost stratum corneum), does not compromise the barrier function of the skin. This is most likely due to the fact that, as a consequence of the small wound dimensions, surface keratinocytes are able to migrate laterally and therefore functionally compensate for those cells that have been destroyed. There is some evidence (see above) that simultaneous epidermal and dermal damage is synergistic in promoting tissue remodeling and promotes myofibroblast differentiation. This is an improvement over existing methods, wherein the skin's barrier function is more severely compromised, increasing susceptibility to infection and dehydration, and slowing re-epithelialization.

Although particular depth ranges of the skin can be targeted to generate a pattern of thermal wounding that does not damage the surface, as described above, it is preferred that the methods and apparatus according to the present invention are employed to induce a pattern of wounding affecting both the superficial epidermis and the deeper dermis. This is particularly useful in situations where treatment is directed toward targets that may be located at varying depths within the skin. For example, when treating vascular disorders, such as port-wine hemangiomas, the blood vessels to be treated may be present at varying depths within the dermis. The methods and apparatus according to the present invention can be used to create micro-lines that are spaced close enough along the surface and extend deep enough into the dermal tissue such that they will damage all of the blood vessels in the dermal tissue of interest to more effectively treat this disorder.

An advantage of the present invention over treatment methods that require selective cooling of the surface to reduce or eliminate damage to the outer surface of the epidermis is that the present method allows for a simpler apparatus that does not require a cooling function. Cooling of the skin surface may optionally be used with various embodiments of the invention disclosed herein to reduce the amount of pain perceived by the person being treated. No surface cooling of the skin is required in some embodiments of the present method and apparatus to achieve the desired wounding patterns. Thus, a further advantage of the present invention is that the operational parameters of the apparatus (such as transverse velocity and power intensity, if any, of the damaging means) can be varied over a wider range

during a treatment procedure. Operating conditions, including characteristics of the applied electromagnetic energy or blades, application of cooling or analgesics for pain control, and the like, are not constrained by restrictive balancing requirements between local heating and cooling effects.

Unlike methods that target a specific range of tissue depths, for example, by focusing of energy and/or selective superficial cooling, some embodiments according to the present invention are directed toward creating micro-lines of damaged tissue extending from the skin surface through the epidermis and dermis using directed energy sources. The resulting damaged regions extend over a broader range of tissue depths within the skin, and creation of these micro-lines is less sensitive to the specific location of the energy sources relative to the skin surface than when using methods that focus damage on specific depths within the dermal tissue. In these embodiments, the directed energy sources need not even contact the surface of the skin to create the desired micro-lines of damaged tissue.

In an embodiment of the present invention, the average energy of each beam of electromagnetic radiation is approximately 0.1-10W. The energy of each beam may also be chosen preferentially in the range of approximately 0.5-3W, or more preferentially approximately 1 W. The energy chosen for a given application depends on the wavelength of energy used, the tissue being treated, and the desired depth of the micro-lines. Average beam energies can be selected outside of the ranges listed above depending on the type of thermal wound characteristics desired.

An advantage of some embodiments according to the present invention is that the micro-line wounding patterns extend over a range of depths within the skin, producing a wound healing effect that is enhanced over that which can be achieved by targeting only a single tissue layer. Producing a continuous micro-line pathway of damage extending from the skin surface down through the epidermis and into the dermis can facilitate the vertical extrusion of necrotic debris, giving rise to beneficial effects including controlled pigment removal.

In one embodiment of the present invention, the micro-lines of damaged tissue may have a depth in a direction normal to the surface of the skin of up to about 1000  $\mu\text{m}$ . In another embodiment, the depth of the micro-lines is up to about 300  $\mu\text{m}$ . If the tissue damage is to be limited primarily to the epidermis, then the depth of the micro-lines may be limited to about 50-100  $\mu\text{m}$ . The depth of the damaged regions may be selected to be any distance less than or about equal to the maximum depth noted, and selection of a particular depth for a given application will depend on the type of results to be achieved by stimulation of wound healing.

When treating a single region of skin, the plurality of micro-lines created may have different depths. Further, the depth of a single micro-line may vary along its length. This may be done to target specific areas within the skin for damage and subsequent healing, or to reduce the density of damage created at deeper levels in the skin.

The width of the micro-lines as measured in a direction parallel to the surface of the skin may be between about 10  $\mu\text{m}$  and 1mm, although it may be preferable to create micro-lines having a width of approximately 30 and 400  $\mu\text{m}$ . It may be even more preferable to create micro-lines having a width of approximately 60 and 120  $\mu\text{m}$ , and it may be most preferable to create micro-lines having a width of approximately 80  $\mu\text{m}$ .

It is preferable for micro-lines of damaged tissue that are created in the dermal tissue to have sufficient undamaged tissue adjacent to them over at least most of their length to promote rapid healing and other beneficial effects, including those as described above. In one embodiment according to the present invention, the average width of the undamaged regions of skin between adjacent micro-lines may be approximately the same as the width of the micro-lines, corresponding to a fractional coverage of the skin with damaged regions of about 50%. In other embodiments according to the present invention, the average width of the undamaged regions of skin between the micro-lines may be as large as approximately two, three, four, or nine times the average width of the adjacent micro-lines, corresponding to fractional coverage of the skin by damaged regions of about 33%, 25%, 20%, and 10%, respectively. In other embodiments according to the present invention, the average width of the undamaged regions of skin between the micro-lines may be as small as approximately two-thirds, one-half, or one-fourth of the average width of the adjacent micro-lines, corresponding to fractional coverage of the skin by damaged regions of about 60%, 67%, and 80%, respectively. The fractional coverage of the skin by damaged regions in other embodiments according to the present invention may include any values lying between the specific ratios of about 10% to 80% noted above. The micro-lines should also be spaced close enough together to provide sufficient density of damaged tissue in the treated area to obtain the desired results.

A variety of micro-line patterns of damaged tissue regions may be created in the dermal tissue of interest while keeping in spirit with the embodiments according to the present invention. Examples of such patterns are shown in, but not limited to, Figs. 4(a)-4(i). In these figures, the width of the micro-lines 210 is approximately the same as the width of the regions of undamaged tissue 215 between them. The ratio of the width of these regions can be varied to achieve the fractional surface coverage of the skin by micro-lines desired.

In one embodiment according to the present invention, a number of essentially parallel micro-lines of damaged tissue 210 may be created as shown in Fig. 4(a). Alternatively, a cross pattern of micro-lines 210 may be created as shown in Fig. 4(b). Such cross patterns will have a larger fractional coverage for a given spacing and width of micro-lines than a non-crossed pattern. Such cross patterns of micro-lines can also be made at any relative angle in addition to the nearly-perpendicular sets of micro-lines shown in Fig. 4(b). In other embodiments, one or more micro-lines 210 may be discontinuous as shown in Fig. 4(c), and Fig. 4(d). These discontinuous micro-lines can be considered as comprising a series of shorter micro-lines. In addition to straight micro-lines, many other patterns may be created. It is within the scope of this invention to create one or more wavy micro-lines 210 as shown in Figs. 4(e) and 4(f). Optionally, curved micro-lines 210 may be created as shown in Fig. 4(g). Such curved lines may be shaped to follow certain contours of the skin being treated or contours of defects in the skin. Other geometric patterns of micro-lines may also be used. For instance, micro-lines 210 having the form of concentric circles may be created, as shown in Fig. 4(h). Alternatively, micro-lines 210 having the shape of a spiral may be formed as shown in Fig. 4(i). Any of the micro-line patterns shown in Figs. 4(e)-(i) may also be formed in a discontinuous pattern similar to that shown in Fig. 4(c).

The length of the micro-lines is preferably at least four to five times the width of the micro-lines at the surface of the skin. The length-to-width ratio of a micro-line may be much larger, with no defined upper limit, and individual micro-lines may traverse the entire region of skin being treated. Some micro-line patterns such as the concentric circles in Fig. 4(h) will not have a clearly defined length-to-width ratio, but nevertheless fall within the scope of the present invention. The anisotropic nature of the micro-line patterns can yield desirable healing results that cannot be achieved with more isotropic or homogeneous patterns such as a distribution of dot-shaped regions of damaged tissue. Micro-line patterns of damage can result in tissue shrinkage and wound healing reactions that vary in the directions parallel to and orthogonal to the micro-lines. It thus is possible to obtain desirable treatment results, for example, by creating a series of micro-lines that are parallel to a set of elongated features such as wrinkles in the skin. Alternatively, optimal treatment results may be obtained in some cases by creating micro-lines that are parallel to elongated features present in the skin. Formation of micro-lines of damaged dermal tissue allows for easier and more uniform application of wound patterns over larger areas of skin than that obtainable by using other patterns.

In one embodiment of the present invention, the micro-lines of damaged tissue may be created by directing a plurality of beams of electromagnetic radiation ('EMR') onto the skin.

Figure 5 illustrates a progressive use of a first exemplary embodiment of a fractional resurfacing apparatus 500 for conducting various dermatological treatments using EMR and generating a pattern of micro-lines of skin damage over a target region of skin according to the present invention. The system 500 may be used for collagen remodeling, removal of unwanted pigment or tattoo, and other dermatological applications. As shown in Fig. 5, the apparatus 500 comprises a case 501, an EMR source 502, a control module 504, and delivery optics 506. The EMR source 502, control module 504, and delivery optics 506 are configured to direct a plurality of discrete beams of electromagnetic radiation 510 towards the epidermis 100. In one embodiment according to the present invention, housing 501 is translated over a region of the skin being treated. This motion of the housing 501 and of the delivery optics 506 contained at least partially therein to create micro-lines of damage 210 in the skin. Preferably, the velocity of the beams of electromagnetic radiation over the tissue being treated is approximately 0.5-10cm/sec, and most preferably about 1-2 cm/sec.

In one exemplary variant according to the present invention, the control module 504 can be in wireless communication with the EMR source 502. In another variant, the control module 504 may be in wired communication with the EMR source 502. In another exemplary variant according to the present invention, the control module 502 can be located outside of the case 501. In another variant, the EMR source 502 is located outside of the case 501. In still another variant, both the control module 504 and the EMR source 502 are located outside of the case 501.

The radiation produced by the EMR source 502 can be optical radiation that is collimated or which may slightly focused, and directed by the delivery optics 506. In one embodiment according to the present invention, the EMR source 502 may comprise, but is not limited to, a diode laser, a diode-pumped solid state laser, an Er:YAG laser, a Nd:YAG laser, an argon-ion laser, a He-Ne laser, a carbon dioxide laser, an excimer laser, or a ruby laser. The beams of radiation produced by the EMR source and directed by the delivery optics may optionally be continuous or pulsed.

In another embodiment of the present invention, each beam 510 has an average energy delivery rate of approximately 1 W and may operate in different wavelengths depending on the application and treatment effect desired. For example, to remove wrinkles it may be preferable to have a laser with a wavelength in the approximate range of 1000-2300 nm. For pigment removal, it may be preferable to have a laser with a wavelength in the approximate range of 400-1000 nm. Water-absorbed wavelengths in the range of 1200-2300 nm may also be used for controlled pigment removal, and it may be preferable in some treatments to employ a

wavelength of up to approximately 3000 nm. In contrast to treatment concepts that rely on a homogeneous electromagnetic radiation (EMR) field delivery, such as conventional selective photothermolysis, the amount of pigment removed by employing the present invention is controlled primarily by the density and depth of the micro-lines rather than by the dosimetry of the beam. Each beam of electromagnetic energy delivered by the delivery optics 506 may be collimated or, alternatively, slightly focused.

The control module 504 provides application specific settings to the EMR source 502. The EMR source 502 receives these settings, and generates EMR based on these settings. The settings can control, *inter alia*, the wavelength and frequency, and the beam profile of the EMR. If the EMR source 502 is pulsed, the control module 504 can also control the pulse duration for each EMR pulse, the fluence of the EMR, the number of EMR pulses, and/or the delay between individual EMR pulses. The control module 504 may be any sort of data processing apparatus that receives, processes, and outputs signals, such as a personal computer, a microprocessor, a microelectronic assembly, or a specially designed control unit.

A preferred exposure time of a local region of skin to radiation delivered by the delivery optics 506 is approximately 1 to 50 ms. The exposure time is determined by the diameter of each beam of energy 510, and by the velocity of beam in a direction parallel to the surface of the skin. If the EMR source is pulsed, the local exposure time is also determined by the pulse rate and duration of the individual pulses. The local exposure time corresponds to the total time required for a beam of energy delivered by the delivery optics 506 to pass over a particular location on the skin. If the exposure time is less than 1 ms there may not be enough local thermal damage to induce wound healing. Exposure times greater than 50 ms may lead to excessive local thermal damage and to negative side effects.

Delivery optics 506 are configured to direct electromagnetic radiation generated by EMR source 502 towards the surface of the skin in the form of a plurality of beams 510. In an embodiment according to the present invention, delivery optics 506 comprises one or more fiber optic guide or other form of waveguide. In other embodiments, delivery optics 506 may further comprise one or more beam splitters, including but not limited to prisms or partially-reflecting mirrors. In variants according to the present invention wherein the EMR source 502 is located outside of the case 501, delivery optics 506, which guide the EMR into the housing 501 and directs it towards the skin, may be located partially outside of housing 501. In one such variant, the delivery optics comprises one or more lengths of flexible optical fiber that originate at EMR source 502 and terminate within housing 501. In this variant, delivery



optics 506 may further comprise one or more beam splitters located within housing 501, and delivery optics 506 are configured to direct a plurality of beams 510 towards the skin.

In an exemplary embodiment according to the present invention, the fractional resurfacing apparatus 500 may optionally include a position sensor, which is in communication with the control module 504. The position sensor is capable of determining the relative velocity between the surface of the skin and the fractional resurfacing apparatus containing the delivery optics 506.. The position sensor can be an optical mouse, one or more wheels, a track ball, a conventional mouse, and the like.

A position sensor can be used as a safety control to optimize the characteristics of the micro-lines formed in practicing the present invention, and also to protect the skin from overexposure to EMR. If the measured velocity of the apparatus along the skin is less than a predetermined velocity, then local exposure times to the energy sources may exceed 50 ms and have a negative impact on the tissue. For example, lateral heat diffusion may result in the transition from a fractional wounding pattern to a contiguous wounding pattern, leading to pronounced side effects including potential scarring.

In one embodiment according to the present invention, the control unit compares the velocity measured by the position sensor with a predetermined velocity during treatment of the skin. If the measured velocity is lower than a predetermined cut-off velocity, then the EMR source 502 is turned off or the EMR delivered by the delivery optics is otherwise interrupted.

In an alternative embodiment, the position sensor may be used in conjunction with the control module 504 to vary the intensity of the EMR provided by the EMR source 502 during treatment of the skin. The intensity of the radiation directed onto the skin by delivery optics 501 may be adjusted to be approximately proportional to the velocity measured by the position sensor, which would result in a more uniform energy density being applied to create each micro-line as the translational velocity of the apparatus 500 over the skin varies.

If the EMR source 502 provides a pulsed source of radiation to delivery optics 506, then control module 504 can be configured to vary the duration and/or frequency of the pulses based on the velocity measured by the position sensor. This represents an alternative method that may be employed to provide better control of the characteristics of the micro-lines formed when practicing embodiments of the invention. Other control methods may be employed in ways known to those skilled in the art and in accordance with the present invention to control the characteristics of the micro-lines by using a position sensor in conjunction with the EMR source 502 and control module 504.

In practicing methods according to the present invention, a range of EMR parameters can be used depending on the desired effects. In one embodiment, EMR parameters may be adjusted such that the temperature of the tissue damaged in the micro-lines is raised sufficiently to stimulate the release of cytokines, heat shock proteins, and other wound healing factors, without stimulating necrotic cell death. In another and preferred embodiment, the EMR parameters are adjusted such that necrotic cell death is induced in the damaged regions of dermal tissue.

In an exemplary embodiment according to the present invention, the case 501 of apparatus 500 shown in Fig. 5 may have a handle attached to it. In this variant, apparatus 500 may be manually translated over the skin such that beams of radiation 510 produce micro-lines of damage in a desired pattern.

In an alternative embodiment of the present invention, apparatus 500 further comprises scanning means capable of directing the beams of electromagnetic energy in a path along the skin being treated while the housing 501 is held essentially stationary with respect to a region of the skin to be treated. The scanning means may comprise a structure such as a platform, or plate that is movably attached to housing 501, and a moving means such as a motor. At least a part of the delivery optics 506 may be mounted to the structure. Alternatively, the scanning means may comprise one or more mirrors configured to reflect the beams of radiation, and a moving means for controllably adjusting the positions and/or angles of the mirrors. In these embodiments, control module 504 or other control means may be employed in conjunction with the scanning means to controllably scan a plurality of beams of radiation 510 across the surface of the skin to create micro-lines of a desired pattern. Mechanisms and control methods for performing this beam scanning function may be chosen from among those known to persons of skill in the art.

In another embodiment of the invention, the micro-line regions of damaged dermal tissue may be created mechanically using a number of diamond knives, microblades, scalpels, or similar cutting means (hereinafter "blades"). Apparatus 600, shown schematically in Figure 6, may be used to create a pattern of micro-lines of tissue damage in accordance with an embodiment of the present invention. Apparatus 600 comprises a plurality of blades 610 mounted to base 620. Blades 610 are mounted at intervals along an axis such that they are uniformly or non-uniformly spaced. The spacing of blades 610 corresponds to the spacing of the micro-lines that can be created using this apparatus. The width of the micro-lines created by this apparatus is determined by the width of the blades 610. The blade width may be the

same for all blades 610, or alternatively one or more blades may have different widths. Apparatus 600 may optionally comprise handle 630.

In this embodiment, apparatus 600 is pressed onto the skin such that the exposed portions of blades 610 penetrate the skin and the lower surface 625 of base 620 contacts the surface of the skin. Apparatus 600 can be manually translated along the region of skin being treated, and blades 610 will form a set of parallel micro-lines in the skin.

The distance that blades 610 protrude from the lower surface 625 of base 620 can determine the depth of the micro-lines formed in accordance with this embodiment of the invention. This distance may be the same for all blades 610, or alternatively one or more blades may protrude different distances from lower surface 625. In another variant, apparatus 600 may also include adjusting means by which the spacing between blades and/or distance by which the exposed portions of blades 610 protrude from surface 625 can be adjusted.

The plurality of blades 610 may also be mounted to a mechanical device movably attached to a frame, and provided with moving means configured to move the device and blades over the area of tissue to be treated. A controller may optionally be employed with such a mechanical device, wherein the controller directs the movement of the blades. Such a controller may be any sort of data processing apparatus that receives, processes, and outputs signals, such as a personal computer, a microprocessor, or a specially designed control unit. The controller may optionally be integrated with the mechanical device apparatus.

In an embodiment according to the present invention, the blades create micro-lines that mechanically damage the epidermis and, optionally, the dermis. Preferably, the blades damage the tissue up to a depth of no more than 1000  $\mu\text{m}$  from the outer surface of the skin, so that there would not be complete separation of the dermis. The blades are moved in a direction along the skin so that they create micro-lines of tissue damage in the skin. The width of the micro-lines may be up to 200  $\mu\text{m}$ . It may be preferable to create micro-lines having a width of approximately 100  $\mu\text{m}$ .

In another embodiment of the invention, the damaging means according to the present invention may be an apparatus comprising one or more blades mounted on a mounting surface, wherein the cutting edges of the blades protrude a defined distance from the lower face of the mounting surface and the cutting edges form a micro-line pattern in a plane parallel to the plane of the mounting surface. This apparatus may be employed to create micro-lines in the skin by a stamping technique, whereby the mounting surface is pressed against the region of skin being treated until the mounting surface contacts the skin surface and then removed. In this manner, micro-lines of damaged tissue can be created mechanically, wherein the depth of the damaged

region is approximately equal to the defined distance that the cutting edges of the blades protrude from the mounting surface, and the pattern and length of the micro-lines formed by each stamping operation is set by the shape of the cutting edges of the blades. The mounting surface may be applied to the dermal tissue of interest manually, wherein the mounting surface may be attached to a handle or some other holding means. Alternatively, the mounting surface may be attached to a mechanical device capable of positioning the mounting surface relative to the dermal tissue of interest and pressing it against the skin.

In any of the mechanical means employing blades described above, the blades and the surface they are attached to may be cooled prior to applying the blades to the skin. This cooling may alleviate any pain felt by the subject of the treatment. The region of skin being treated may also be cooled before the blades are positioned to penetrate the skin. In another variant, a topical analgesic may be applied.

Fractional resurfacing may cause portions of the epidermis to be thermally damaged or ablated, thereby reducing the efficacy of the barrier function of the epidermis and in particular decreasing the stratum corneum. This facilitates the delivery of drugs or specific substances to the dermis and epidermis, which can either enhance the effects of the treatment, or decrease the side effects caused by partial damage of the epidermis and/or dermis. Groups of drugs and substances, which may enhance the efficacy of skin remodeling include growth factors, collagen byproducts, collagen precursors, hyaluronic acid, vitamins, antioxidants, amino acids and supplemental minerals among others. Groups of drugs and substances, which may decrease side effects, can be steroidal anti-inflammatory drugs, non-steroidal anti-inflammatory drugs, antioxidants, antibiotics, antiviral drugs, antiyeast drugs and antifungal drugs. In an exemplary embodiment of the present invention, the vitamins that are used may be vitamin C and/or vitamin E. The supplemental minerals used are copper and zinc. The antioxidants can be vitamin C and/or vitamin E.

Other embodiments of the present invention include methods of applying or gluing a specific disposable mask (a thin layer of material that may be continuous or discontinuous) to a region of the skin before creating micro-lines of damaged tissue. The optional use of such a mask may achieve several purposes. Individually embedded wires or mechanically enforced structures within the mask may be used to guide the damaging means and to ensure that the desired micro-line pattern is provided. A superficial guidance system incorporated in the mask may also be implemented to guide the treatment process. Also, the mask or layer may incorporate markers embedded in a spatial pattern that helps to determine the scanning velocity and the positioning of the damaging means.

Application of a mask in accordance with the present invention may also improve mechanical stability of the tissue (by acting as a wound dressing) after formation of the micro-lines. The mask may be also medially compounded or provided with embedded microchambers in order to release desired materials (e.g. analgesics, wound healing promoters, antibiotics or other modulators) into the tissue during or before the wounding process. The mask may comprise a polymer having a specific memory of contraction that may be activated by the treatment or which applies a continuous (directed) tension after wounding to direct the wound healing and remodeling process.

Several designs of a mask that provides “immediately sealing wound dressing” can be implemented in accordance with the present invention. In one embodiment, an apparatus having a plurality of blades is employed to mechanically produce micro-lines of damage. The blades cut through a thin mask which is glued to or otherwise attached to the skin, and immediately after this cutting a fast hardening glue is sprayed to the surface. Alternatively a tape having adhesive or adhering qualities may be rolled over the thin mask immediately after cutting. This tape may shrink in a well-defined way after coming into contact with the thin mask that is attached to the skin to help close the cut micro-lines and promote healing.

Having thus described in detail preferred embodiments of the present invention, it is to be understood that the invention defined by the above paragraphs is not to be limited to particular details set forth in the above description as many apparent variations thereof are possible without departing from the spirit or scope of the present invention.

WHAT IS CLAIMED IS:

1. A method for treating skin, said method including:  
providing a skin damaging means;  
applying said damaging means to create a plurality of micro-lines of damaged tissue in a region of skin separated by regions of undamaged skin tissue, wherein said micro-lines are substantially parallel and traverse at least part of said region of skin being treated.
2. The method of claim 1, wherein said damaging means comprises one or more beams of electromagnetic radiation.
3. The method of claim 1 or 2, wherein the source of said electromagnetic radiation comprises a laser, a diode laser, a ER:YAG laser, a Nd:YAG laser, an argon-ion laser, a He-Ne laser, a carbon dioxide laser, an excimer laser, or a ruby laser.
4. The method of any one of claims 1 to 3, wherein the source of said electromagnetic radiation further comprises a beam splitter.
5. The method of any one of claims 2 to 4, wherein the wavelength of the electromagnetic radiation is between approximately 400 nm and 1000 nm, or between approximately 1200nm and 2300 nm.
6. The method of any one of claims 2 to 5, wherein the average energy of each beam of electromagnetic radiation is approximately 0.1-10W, approximately 0.5-3W, or approximately 1 W.
7. The method of any one of claims 1 to 6, wherein said damaging means comprises a plurality of blades, scalpels, diamond knives, or other cutting means.
8. The method of any one of claims 1 to 7, wherein said micro-lines of damaged tissue extend into the skin to a depth of up to 50-1000  $\mu\text{m}$ .
9. The method of any one of claims 1 to 8, wherein the width of said micro-lines of damaged tissue at the skin surface is between about 10  $\mu\text{m}$  and 1 mm, between about 30  $\mu\text{m}$  and 400  $\mu\text{m}$ , between about 60  $\mu\text{m}$  and 120  $\mu\text{m}$ , or approximately 80  $\mu\text{m}$ .
10. The method of any one of claims 1 to 9, wherein the width of undamaged skin tissue between adjacent micro-lines at the skin surface is approximately equal to the width of the adjacent micro-lines.
11. The method of any one of claims 1 to 10, wherein the width of undamaged skin tissue between adjacent micro-lines is between about 10  $\mu\text{m}$  and 1 mm, between about 30  $\mu\text{m}$  and 400  $\mu\text{m}$ , between about 60  $\mu\text{m}$  and 120  $\mu\text{m}$ , or approximately 80  $\mu\text{m}$ .

12. The method of any one of claims 1 to 11, wherein the width of undamaged skin tissue between adjacent micro-lines at the skin surface is approximately equal to twice the width of the adjacent micro-lines.

13. The method of any one of claims 1 to 12, wherein the width of undamaged skin tissue between adjacent micro-lines is between about 20  $\mu\text{m}$  and 2 mm, between about 60  $\mu\text{m}$  and 800  $\mu\text{m}$ , between about 120  $\mu\text{m}$  and 240  $\mu\text{m}$ , or approximately 160  $\mu\text{m}$ .

14. The method of any one of claims 1 to 13 wherein the micro-lines form a trace on the surface of the skin being treated that is a set of essentially parallel straight lines, essentially parallel curved lines, or essentially parallel wavy lines.

15. The method of any one of claims 1 to 14 wherein at least a portion of the surface of said region of skin is superficially cooled before creation of said micro-lines and, optionally, cooled during creation of said micro-lines.

16. The method of claim 15 wherein at least a portion of said region of skin is superficially cooled by conductive or convective means.

17. An apparatus for treating skin, comprising:  
a housing;  
one or more sources of electromagnetic radiation;  
an optical delivery system located at least partially within said housing,  
configured to direct a plurality of beams of said electromagnetic radiation onto the skin being treated to create a plurality of micro-lines of damaged tissue that traverse a region of skin being treated; and  
a control module capable of controlling the characteristics of the electromagnetic radiation generated by said source of electromagnetic radiation.

18. The apparatus of claim 17 wherein said source of electromagnetic radiation comprises one or more of a laser, a diode laser, a ER:YAG laser, a Nd:YAG laser, an argon-ion laser, a He-Ne laser, a carbon dioxide laser, an excimer laser, or a ruby laser

19. The apparatus of claim 17 or 18 wherein said beams of electromagnetic radiation are pulsed.

20. The apparatus of any one of claims 17 to 19 wherein said optical delivery system further comprises a beam splitter.

21. The apparatus of any one of claims 17 to 20, wherein the wavelength of the electromagnetic radiation is between approximately 400 nm and 1000 nm, or between approximately 1200nm and 2300 nm.

22. The apparatus of any one of claims 17 to 21, wherein said beams of electromagnetic radiation are collimated or slightly focused.

23. The apparatus of claim 22, wherein the diameter of said beams of electromagnetic radiation at the surface of the region of skin being treated is between about 10  $\mu\text{m}$  and 1 mm, between about 30  $\mu\text{m}$  and 400  $\mu\text{m}$ , between about 60  $\mu\text{m}$  and 120  $\mu\text{m}$ , or approximately 80  $\mu\text{m}$ .

24. The apparatus of any one of claims 17 to 23, wherein the average energy of each of said beams of electromagnetic radiation is approximately 1 W.

25. The apparatus of any one of claims 17 to 24 further comprising a position sensor capable of detecting the velocity of said beams of electromagnetic radiation along the skin, and wherein said position sensor is configured to provide signals to said control module.

26. The apparatus of claim 25, wherein said control module is configured to shut off said source of electromagnetic radiation or otherwise interrupt said beams of electromagnetic radiation when the velocity of said beams across the surface of said region of skin falls below a predetermined value.

27. The apparatus of claim 25 or 26, wherein said control module, position sensor, and source of electromagnetic radiation are configured to vary the intensity of said beams of electromagnetic radiation in proportion to the velocity at which said beams traverse the surface of said region of skin.

28. The apparatus of any one of claims 25 to 27, wherein said beams of electromagnetic radiation are pulsed, and said controller is configured to vary the pulse frequency or pulse duration of said beams of electromagnetic radiation in relation to the velocity at which said beams traverse the surface of said region of skin.

29. The apparatus of any one of claims 17 to 28 wherein said beams of electromagnetic radiation are spaced such that said plurality of micro-lines of damaged tissue cover approximately 50%, 40%, 30%, or 20% of the surface of said region of skin being treated.

30. The apparatus of any one of claims 17 to 29 wherein said housing further comprises a handle and is configured to be manually traversed over said region of skin being treated to form said micro-lines of damaged tissue.

31. The apparatus of any one of claims 17 to 30 further comprising a scanning means configured to scan said beams of electromagnetic radiation over a region of skin to be treated to create a plurality of micro-lines of damaged tissue, with said housing being held essentially stationary relative to said region of skin being treated.



32. The apparatus of any one of claims 17 to 31 wherein said housing further comprises conductive cooling means capable of cooling the surface of said skin being treated before or during the creation of said micro-lines of damaged tissue.

33. The apparatus of any one of claims 17 to 32 wherein said housing further comprises convective cooling means capable of cooling the surface of said skin being treated before or during the creation of said micro-lines of damaged tissue.

34. An apparatus for treating skin, comprising:  
a housing;  
a mounting surface attached to said housing; and  
a plurality of essentially parallel blades fixed to said mounting surface,  
wherein said blades are configured to protrude from said mounting surface and penetrate the skin to create a plurality of micro-lines of damaged tissue when said housing is translated over a region of skin being treated.

35. The apparatus of claim 34 wherein said blades comprise diamond knives, microblades, or scalpels.

36. The apparatus of claim 34 or 35 wherein said blades are configured to penetrate into said skin to a depth of up to 1000  $\mu\text{m}$ , up to 300  $\mu\text{m}$ , up to 100  $\mu\text{m}$ , or up to 50  $\mu\text{m}$ , when said housing is translated over said region of skin being treated.

37. The apparatus of claim 36 wherein the maximum width of said blades is approximately 30  $\mu\text{m}$ , approximately 60  $\mu\text{m}$ , approximately 80  $\mu\text{m}$ , approximately 120  $\mu\text{m}$ , or approximately 400  $\mu\text{m}$ .

38. The apparatus of claim 37 wherein the spacing between the nearest sides of adjacent blades is approximately 30  $\mu\text{m}$ , approximately 60  $\mu\text{m}$ , approximately 80  $\mu\text{m}$ , approximately 120  $\mu\text{m}$ , or approximately 400  $\mu\text{m}$ .

39. The apparatus of any one of claims 34 to 38 wherein said mounting surface further comprises conductive cooling means configured to contact the surface of said region of skin being treated when said essentially parallel blades are penetrating said skin.

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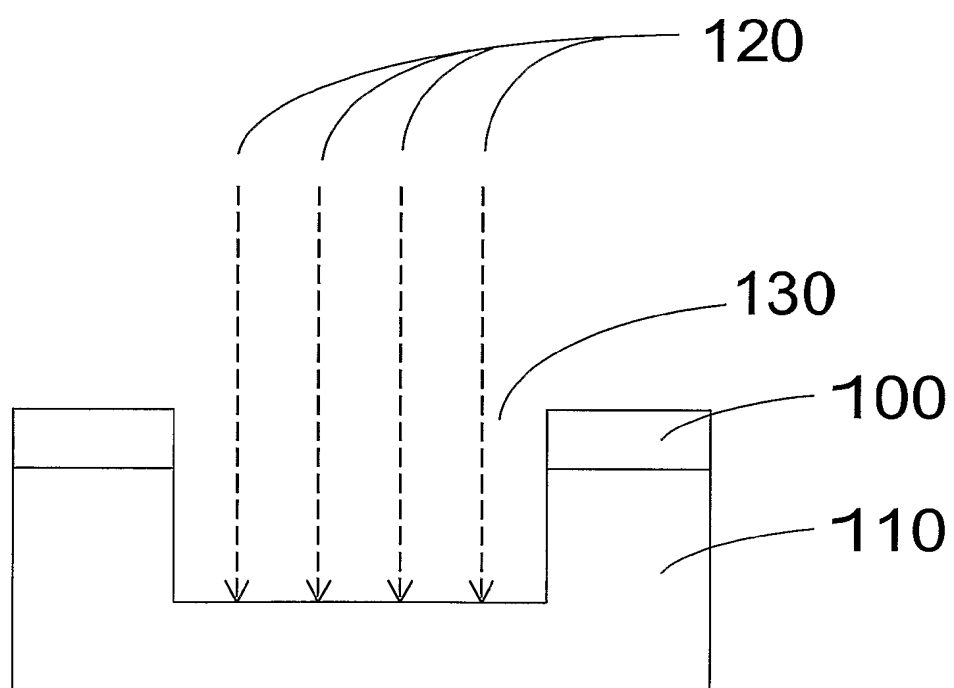


FIG. 1

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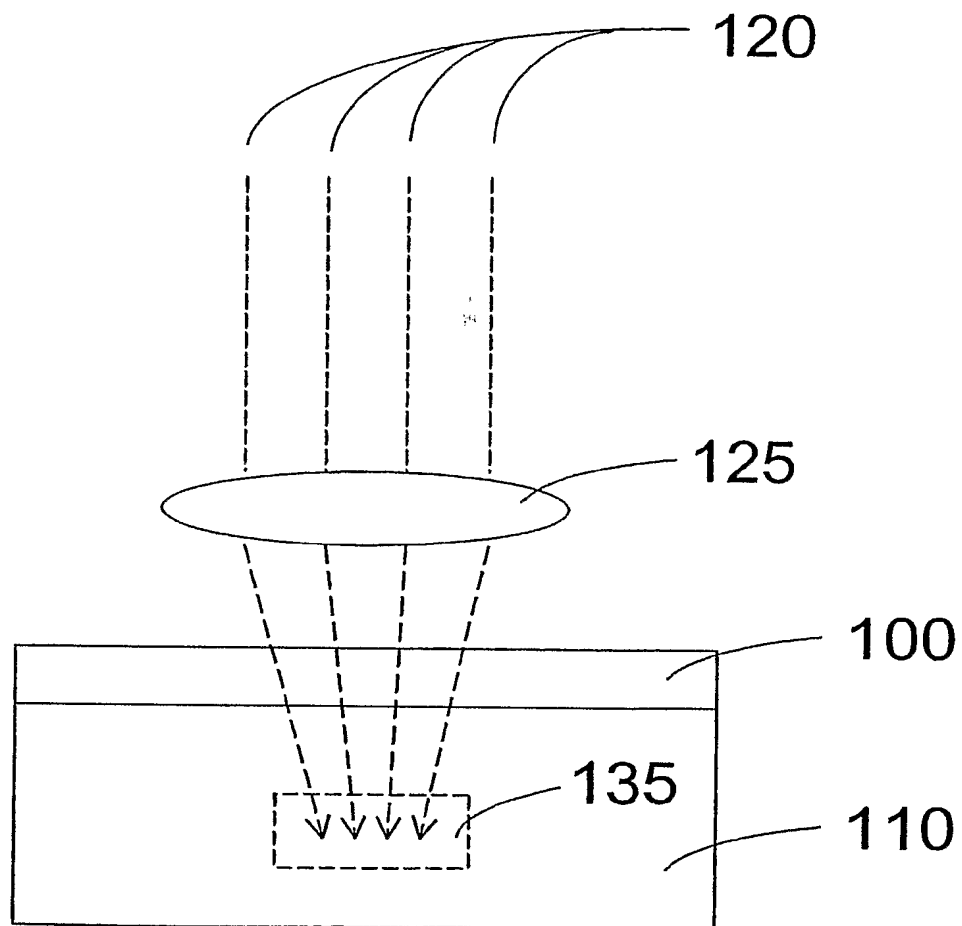


FIG. 2

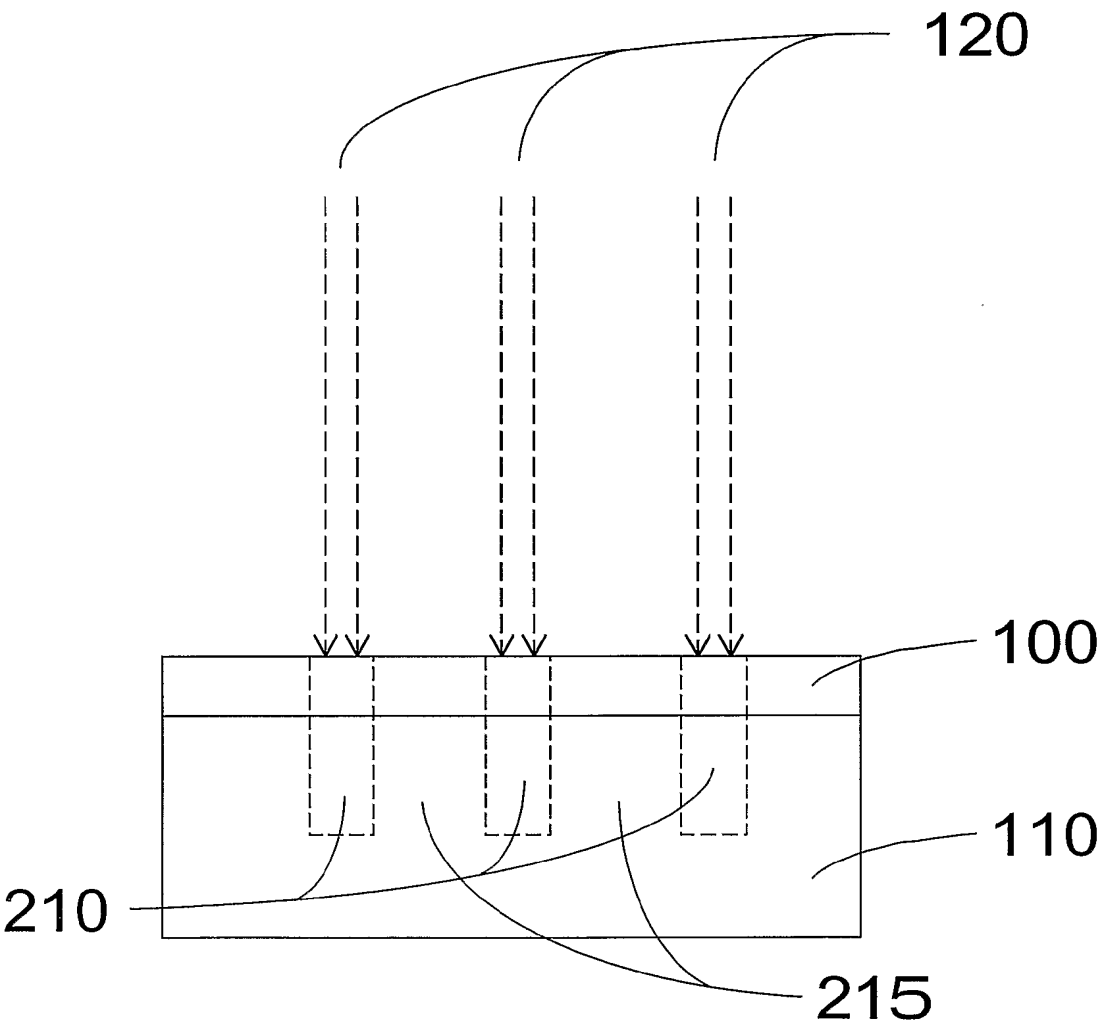


FIG. 3

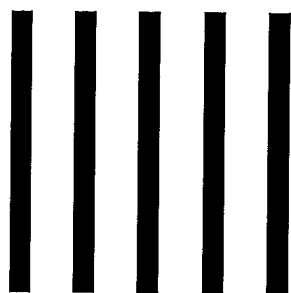


FIG. 4(a)

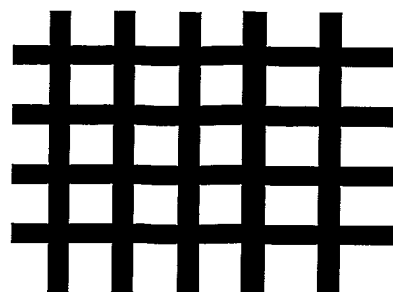


FIG. 4(b)

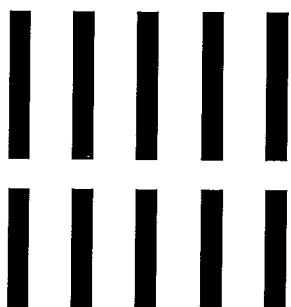


FIG. 4(c)

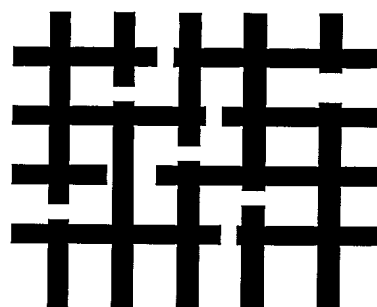


FIG. 4(d)

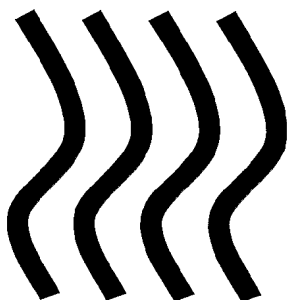


FIG. 4(e)

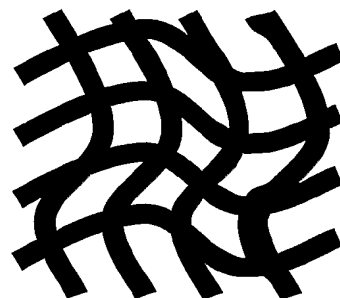


FIG. 4(f)

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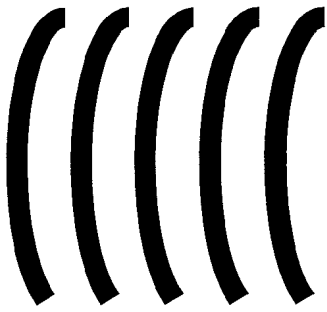


FIG. 4(g)

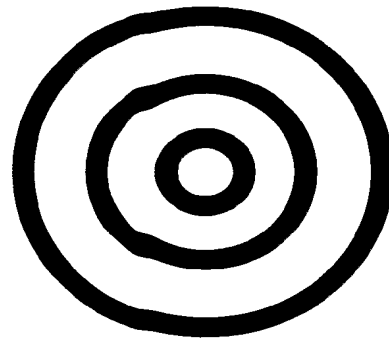


FIG. 4(h)



FIG. 4(i)

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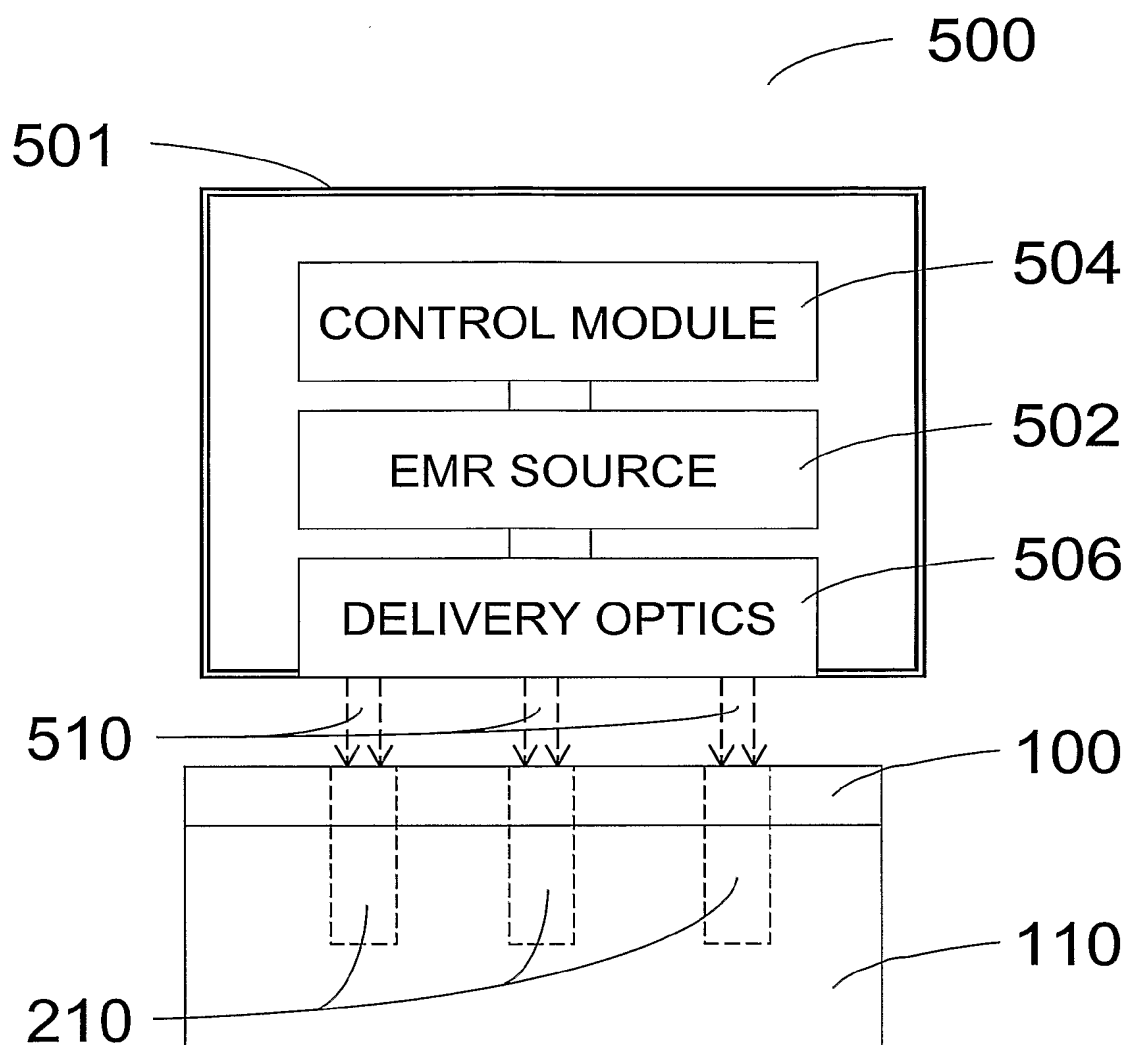


FIG. 5

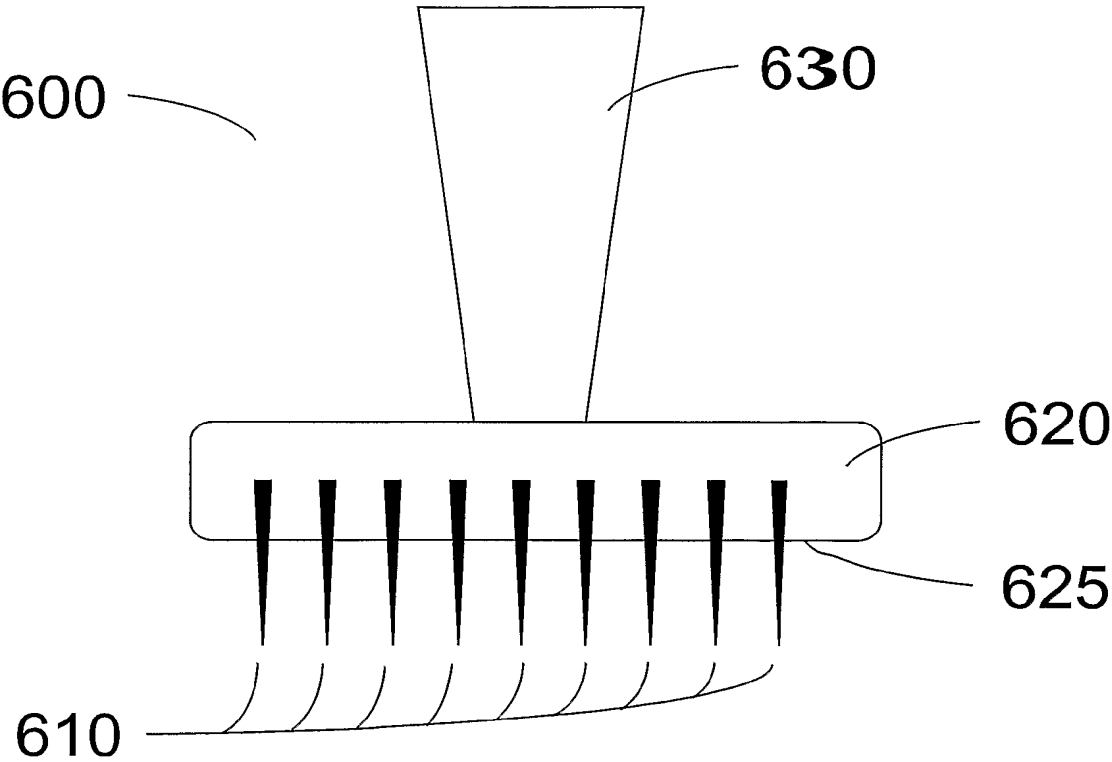


FIG. 6



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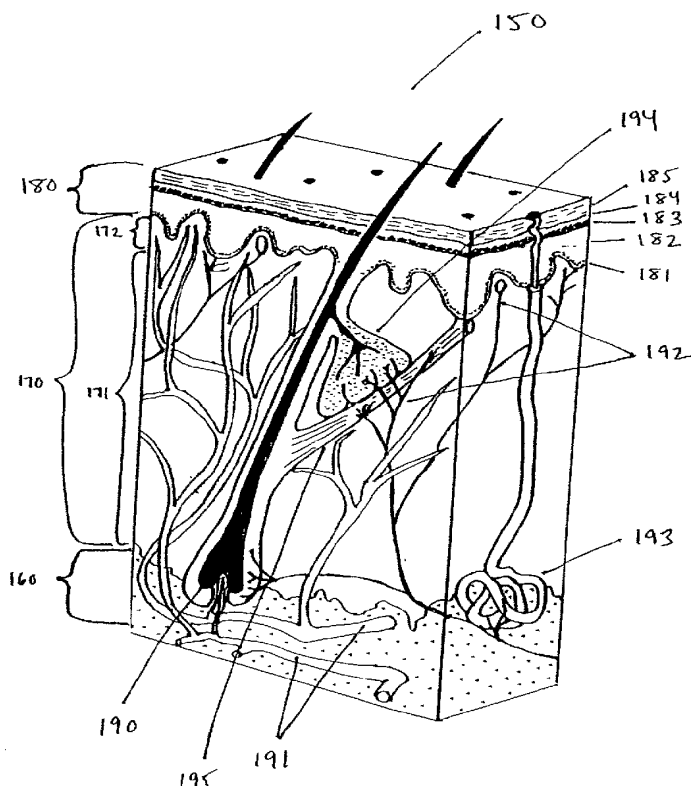
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[Continued on next page]

(54) Title: METHODS AND PRODUCTS FOR PRODUCING LATTICES OF EMR-TREATED ISLETS IN TISSUES, AND USES THEREFOR



(57) Abstract: Methods of treatment of tissue with electromagnetic radiation (EMR) to produce lattices of EMR-treated islets in the tissue are disclosed. Also disclosed are devices and systems for producing lattices of EMR-treated islets in tissue, and cosmetic and medical applications of such devices and systems.



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**METHODS AND PRODUCTS FOR PRODUCING  
LATTICES OF EMR-TREATED ISLETS  
IN TISSUES, AND USES THEREFOR**

RELATED APPLICATIONS

This application claims benefit of priority to U.S. Provisional Application No. 60/561,052, filed April 9, 2004, U.S. Provisional Application No. 60/614,382, filed September 29, 2004, and U.S. Provisional Application No. 60/641,616, filed January 5, 2005; is a continuation-in-part of U.S. Patent Application No. 10/465,137, filed June 19, 2003, which claims benefit of priority to U.S. Provisional Application No. 60/389,871, filed June 19, 2002; is a continuation-in-part of U.S. Patent Application No. 10/033,302, filed December 27, 2001, which claims benefit of priority to U.S. Provisional Application No. 60/258,855, filed December 28, 2000; and is a continuation-in-part of U.S. Patent Application No. 10/080,652, filed February 22, 2002, which claims priority to U.S. Provisional Application No. 60/272,745, filed March 2, 2001.

BACKGROUND OF THE INVENTION

Field of the Invention.

The invention relates to the treatment of tissue with electromagnetic radiation (EMR) to produce lattices of EMR-treated islets in the tissue. The invention also relates to devices and systems for producing lattices of EMR-treated islets in tissue, and cosmetic and medical applications of such devices and systems.

Description of the Related Art

Electromagnetic radiation, particularly in the form of laser light, has been used in a variety of cosmetic and medical applications, including uses in dermatology, dentistry, ophthalmology, gynecology, otorhinolaryngology and internal medicine. For most dermatological applications, the EMR treatment can be performed with a device that delivers the EMR to the surface of the targeted tissues. For applications in internal medicine, the EMR treatment is typically performed with a device that works in combination with an endoscope or catheter to deliver the EMR to internal surfaces and

tissues. As a general matter, the EMR treatment is typically designed to (a) deliver one or more particular wavelengths (or a particular continuous range of wavelengths) of EMR to a tissue to induce a particular chemical reaction, (b) deliver EMR energy to a tissue to cause an increase in temperature, or (c) deliver EMR energy to a tissue to damage or destroy cellular or extracellular structures.

Until recently, all photothermal applications of light in medicine have been based on one of three approaches. The first approach, known as the principle of selective photothermolysis, sets specific requirements for the wavelengths used (which need to be absorbed preferentially by chromophores in the target area) and for the duration of the optical pulse (which needs to be shorter than characteristic thermal relaxation time of the target area). This approach was later extended, and is often called the extended theory of selective photothermolysis, to encompass situations in which the target area and target chromophore are physically separated. The second approach relies on heat diffusion from the target chromophore to the target area. The third approach relies on absorption by a chromophore which is substantially uniformly present in the tissue (*e.g.*, water). In this last case, the damage zone can, in principle, be controlled by manipulating wavelength, fluence, incident beam size, pulse width, and cooling parameters. All three approaches have drawbacks, the most significant of which is the difficulty in eliminating unwanted side effects. Usually, primary absorption of optical energy by water causes bulk tissue damage.

Examples of typical applications in photodermatology include the treatment of dyschromia (skin tone) and skin remodeling. The standard approach to treating dyschromia uses selective absorption of light by melanin in a pigmented lesion or by hemoglobin in blood vessels. A number of lasers and spectrally filtered arc-discharge lamps have been used for such treatments. Usually, the endpoint of treatment is the coagulation of vessels and pigmented lesions. The thermal stress to these targets causes vessels to collapse and die, and pigmented lesions to crust over followed by sloughing-off of the dead skin. In both cases, the skin tone is improved and, as a side effect of such treatment, skin remodeling can occur as the thermal stress to tissues surrounding the blood vessels and pigmented lesions can stimulate new collagen production. These

treatment applications are generally safe due to the limitation of the damage to small structures such as vessels and melanin-containing spots.

One problem with selective photothermolysis is that the wavelength selected for the radiation is generally dictated by the absorption characteristics of the chromophore and may not be optimal for other purposes. Skin is a scattering medium, but such scattering is far more pronounced at some wavelengths than at others. Unfortunately, wavelengths preferentially absorbed by melanin, for example, are also wavelengths at which substantial scattering occurs. This is also true for the wavelengths typically utilized for treating vascular lesions. Photon absorption in skin also varies over the optical wavelength band, and some wavelengths typically used in selective photothermolysis are wavelengths at which skin is highly absorbent. The fact that wavelengths typically utilized for selective photothermolysis are highly scattered and/or highly absorbed limits the ability to selectively target body components and, in particular, limits the depths at which treatments can be effectively and efficiently performed. Further, much of the energy applied to a target region is either scattered and does not reach the body component undergoing treatment, or is absorbed in overlying or surrounding tissue. This low efficiency for such treatments means that larger and more powerful EMR sources are required in order to achieve a desired therapeutic result. However, increasing power generally causes undesired and potentially dangerous heating of tissue. Thus, increasing efficacy often decreases safety, and additional cost and energy must be utilized to mitigate the effects of this undesired tissue heating by surface cooling or other suitable techniques. Heat management for the more powerful EMR source is also a problem, generally requiring expensive and bulky water circulation or other heat management mechanisms. A technique which permits efficacious power levels and minimizes undesired heating is therefore desirable.

Photodermal treatments are further complicated because chromophore concentrations in a target (e.g., melanin in hair follicles) varies significantly from target to target and from patient to patient, making it difficult to determine optimal, or even proper, parameters for effective treatment of a given target. High absorption by certain types of skin, for example dark skinned individuals or people with very tanned skin, often makes certain treatments difficult, or even impossible, to safely perform. A technique

which permits all types and pigmentations of skin to be safely treated, preferably with little or no pain, and preferably using substantially the same parameters, is therefore desirable.

Absorption of optical energy by water is widely used in two approaches for skin remodeling: ablative skin resurfacing, typically performed with either CO<sub>2</sub> (10.6 $\mu$ ) or Er:YAG (2.94  $\mu$ ) lasers, and non-ablative skin remodeling using a combination of deep skin heating with light from Nd:YAG (1.34  $\mu$ ), Er:glass (1.56 $\mu$ ) or diode laser (1.44 $\mu$ ) and skin surface cooling for selective damage of sub-epidermal tissue. Nevertheless, in both cases, a healing response of the body is initiated as a result of the limited thermal damage, with the final outcome of new collagen formation and modification of the dermal collagen/elastin matrix. These changes manifest themselves in smoothing out rhytides and general improvement of skin appearance and texture (often referred to as "skin rejuvenation"). The principal difference between the two techniques is the region of body where damage is initiated. In the resurfacing approach, the full thickness of the epidermis and a portion of upper dermis are ablated and/or coagulated. In the non-ablative approach, the zone of coagulation is shifted deeper into the tissue, with the epidermis being left intact. In practice, this is achieved by using different wavelengths: very shallow-penetrating ones in the ablative techniques (absorption coefficients of  $\sim 900\text{ cm}^{-1}$  and  $\sim 13000\text{ cm}^{-1}$  for CO<sub>2</sub> and Er:YAG wavelengths, respectively) and deeper-penetrating ones in the non-ablative modalities (absorption coefficients between 5 and 25  $\text{cm}^{-1}$ ). In addition, contact or spray cooling is applied to skin surface in non-ablative techniques, providing thermal protection for the epidermis. Resurfacing techniques have demonstrated significantly higher clinical efficacy. One drawback, which severely limited popularity of this treatment in the recent years, is a prolonged post-operative period requiring continuous care. Non-ablative techniques offer considerably reduced risk of side effects and are much less demanding on post-operative care. However, clinical efficacy of the non-ablative procedure is often unsatisfactory. The reasons for such differences in the clinical outcomes of the two procedures are not completely understood. However, one possibility is that damage (or lack thereof) to the epidermis may be an important factor determining both safety and efficacy outcomes. Obviously, destruction of the protective outer epidermal barrier (in particular, the stratum corneum)

in the course of ablative skin resurfacing increases chances of wound contamination and potential complications. At the same time, release of growth factors (in particular, TGF- $\alpha$ ) by epidermal cells have been shown to play a crucial role in the wound healing process and, therefore, in the final skin remodeling. Clearly, this process does not occur if the epidermis is intact.

### SUMMARY OF THE INVENTION

The present invention depends, in part, upon the discovery that, when using electromagnetic radiation (EMR) to treat tissues, there are substantial advantages to producing lattices of EMR-treated islets in the tissue rather than large, continuous regions of EMR-treated tissue. The lattices are periodic patterns of islets in one, two or three dimensions in which the islets correspond to local maxima of EMR-treatment of tissue. The islets are separated from each other by non-treated tissue (or differently- or less-treated tissue). The EMR-treatment results in a lattice of EMR-treated islets which have been exposed to a particular wavelength or spectrum of EMR, and which is referred to herein as a lattice of "optical islets." When the absorption of EMR energy results in significant temperature elevation in the EMR-treated islets, the lattice is referred to herein as a lattice of "thermal islets." When an amount of energy is absorbed that is sufficient to significantly disrupt cellular or intercellular structures, the lattice is referred to herein as a lattice of "damage islets." When an amount of energy (usually at a particular wavelength) sufficient to initiate a certain photochemical reaction is delivered, the lattice is referred to herein as a lattice of "photochemical islets." By producing EMR-treated islets rather than continuous regions of EMR-treatment, more EMR energy can be delivered to an islet without producing a thermal islet or damage islet, and/or the risk of bulk tissue damage can be lowered.

Thus, in various aspects, the invention provides improved devices and systems for producing lattices of EMR-treated islets in tissues, and improved cosmetic and medical applications of such devices and systems

In one aspect, the invention provides methods for increasing the permeability of the stratum corneum of the skin of a subject to a compound by applying EMR radiation to the stratum corneum to produce a lattice of EMR-treated islets. In particular, the invention provides methods for increasing the permeability of the stratum corneum by

treating the stratum corneum with an EMR-treatment device that produces a lattice of EMR-treated islets the stratum corneum, in which the lattice of EMR-treated islets is heated to a temperature sufficient to increase the permeability of the stratum corneum to the compound. In some embodiments, there is a therapeutic agent such as a hormone, a steroid, a non-steroidal anti-inflammatory drug, an anti-neoplastic agent, an antihistamine or an anesthetic agent. In specific embodiments, the therapeutic agent is insulin, estrogen, prednisolone, loteprednol, ketorolac, diclofenac, methotrexate, a histamine H1 antagonists, chlorpheniramine, pyrillamine, mepyramine, emedastine, levocabastine or lidocaine. In some embodiments, the compound is a cosmetic agent such as a pigment, reflective agent or photoprotectant. In general, the lattice of EMR-treated islets is heated to a temperature sufficient to at least partially melt a crystalline lipid extracellular matrix in the stratum corneum. In some embodiments, the increase in permeability is reversible. In some embodiments, the stratum corneum remains damaged until it is replaced by new growth.

In another aspect, the invention provides methods of transdermal delivery of a compound to a subject by treating a portion of the stratum corneum of the subject with an EMR-treatment device that produces a lattice of EMR-treated islets heated to a temperature sufficient to increase the permeability of the stratum corneum to the compound.

In some embodiments, the invention provides methods for increasing the permeability of the stratum corneum by using an EMR-treatment device that delivers EMR energy to endogenous chromophores (*e.g.*, water, lipid, protein) in the tissue. In other embodiments, the EMR-treatment device delivers EMR energy to exogenous EMR-absorbing particles in contact with the tissue.

In another aspect, the invention provides methods for selectively damaging a portion of tissue in a subject by applying EMR radiation to produce a lattice of EMR-treated islets which absorb an amount of EMR sufficient to damage the tissue in the EMR-treated islets but not sufficient to cause bulk tissue damage. In some embodiments, the damage is coagulation or denaturation of intracellular or extracellular proteins in the EMR-treated islets. In other embodiments, the damage is killing of cells or ablation of tissue.



In another aspect, the invention provides methods of producing lattices of damage islets in a tissue in order to treat various pathological conditions of a tissue. For example, in some embodiments, a lattice of damage islets is produced to cause damage to tissues in a wart, a callus, a psoriasis plaque, a sebaceous gland (to treat acne), a sweat gland (to treat body odor), fat tissue, or cellulite.

In another aspect, the invention provides methods of reducing pigment in the skin of a subject by treating a portion of the skin with an EMR-treatment device that produces a lattice of EMR-treated islets in at least one volume of tissue containing the pigment, whereby the pigment is destroyed without killing cells including the pigment. In another aspect, the invention provides methods of reducing pigment in the skin of a subject by treating a portion of the skin with an EMR-treatment device that produces a lattice of EMR-treated islets in at least one volume of tissue containing the pigment, whereby cells including the pigment are destroyed. In any of these embodiments, the pigment can be present in a tattoo, port wine stain, birthmark, or freckle.

In another aspect, the invention provides methods for skin rejuvenation, skin texturing, hypertrophic scar removal, skin lifting, stretch mark removal, non-skin-surface texturing (*e.g.* lip augmentation), and improved wound and burn healing by treating a portion of tissue of a subject with an EMR-treatment device that produces a lattice of EMR-treated damage islets in a desired treatment area and thereby activates an natural healing and/or repair process which improves the desired tissue characteristic.

In another aspect, the invention provides methods for photodynamic therapy of a subject in need thereof, by treating a portion of tissue of the subject with an EMR-treatment device that produces a lattice of EMR-treated islets in a desired treatment area and activates a photodynamic agent present in the islets. In some embodiments, the photodynamic agent is administered to the subject prior to treatment. In some embodiments, the photodynamic agent is an antineoplastic agent or a psoralen.

In the various embodiments of the invention, the lattices of EMR-treated islets can include a multiplicity of islets in which each islet has a maximum dimension of 1  $\mu\text{m}$  to 30 mm, 1  $\mu\text{m}$  to 10  $\mu\text{m}$ ,  $\mu\text{m}$  to 100  $\mu\text{m}$ , 100  $\mu\text{m}$  to 1 mm, 1 mm to 10 mm, or greater. In addition, the lattices can have fill factors of 0.01-90%, 0.01-0.1%, 0.1-1%, 1-10%, 10-30%, 30-50%, or greater. In addition, the lattices of islets can have minimum depths

from the surface of a tissue of 0-4 mm, 0-50  $\mu\text{m}$ , 50-500  $\mu\text{m}$ , or 500  $\mu\text{m}$  - 4 mm, as well as sub-ranges within these.

In the various embodiments of the invention, the lattices of EMR-treated islets can be heated to temperatures of 35-40°C, 40-50°C, 50-100°C, 100-200°C, or greater than 200°C. In some embodiments, the papillary dermis is not heated to a temperature above 40-43°C to prevent pain. In some embodiments, the upper layers of the tissue are cooled to reduce heating of those layers and/or produce subsurface thermal or damage islets.

In another series of aspects, the invention provides devices and systems for practicing the methods of the invention.

This, in one aspect of the invention is an apparatus for performing a treatment on a target area of a patient's skin in order to create treatment islets. According to this aspect, the apparatus features a housing that defines a target treatment area on the patient's skin when placed in proximity to the patient's skin, and an LED or diode laser bar mounted within the housing. The LED or diode laser bar can be used to apply optical energy to the target area. The LED or diode laser bar includes multiple emitters of optical energy for creating treatment islets in the patient's skin. The emitters can be spaced apart by varying amounts. In one aspect, the emitters are spaced apart by about 50 to 900  $\mu\text{m}$ . The width of the emitters can also vary. In some aspects, the widths are about 50 to 150  $\mu\text{m}$ . In some aspects, the emitters can be within about 50 to 1000 microns of the patient's skin, allowing the emitters to create treatment islets. The emitters can emit light in a variety of wavelengths, including, for example, in the wavelength range of about 290 to 10,000 nm. The diode laser bar can include any number of emitters. Some embodiments use between 10 and 25 emitters. Other embodiments can include multiple LEDs or diode laser bars in a hand piece to form a stack.

The apparatus set forth above can also include a variety of other components, such as, for example, a cooling element or a heating element attached to the housing. A cooling element can be disposed between the diode laser bar and the patient's skin when in use to cool the patient's skin. A heating element, on the other hand, can heat the patient's skin. In both cases, the element can allow passage of at least a portion of the

optical energy from the LED or diode laser bar. The cooling or heating element can be made from, for example, sapphire or diamond.

The apparatus set forth above can also include a motor to move the diode laser bar with respect to the housing. The apparatus can include circuitry to vary the control of the motor to move the diode laser bar or LED in a direction opposite to a direction of movement of the housing across the patient's skin.

The apparatus set forth above can, in some aspects, include a mechanism coupled to the emitters for creating treatment islets in the patient's skin. This mechanism can be, for example, a lens array. The mechanism can also be a bundle of optical fibers, wherein each fiber is connected to at least one emitter.

The apparatus set forth above can be, in some aspects, a hand held device. The hand held device can be a hand held dermatological device that includes, for instance, control switches and a button to activate the diode laser bar or LED. The hand held device can be a stand-alone device or can be a device that communicates via an umbilical cord with a base unit.

Another aspect of the invention is an apparatus for performing a treatment on a target area of a patient's skin by applying optical energy on the target area. According to this aspect, the apparatus includes an optical energy source, an applicator movable to a position proximate the target area of the patient's skin for applying optical energy to the target area, and one or more optical fibers for transmitting optical energy from the optical energy source to the applicator. The applicator can include a mechanism for delivering optical energy onto the target area in order to create islets of treatment. The mechanism can be, for example, a total internal reflection element. The optical energy source can be either a coherent or a non-coherent light source.

Another aspect of the invention is a handheld dermatological device. In this aspect, the device includes a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, and a plurality of optical fibers within the housing to couple radiation from a radiation source through the hand piece to the person's skin. In this aspect, the optical fibers can be spaced apart to output radiation to create treatment islets.

Another embodiment of the invention can be an apparatus for treating skin that includes a speed sensor. In this aspect, the apparatus features a light emitting assembly for applying optical energy to the target area of the patient's skin, the light emitting assembly including a head portion movable across the target area of the patient's skin and an optical energy source for outputting optical energy from the light emitting assembly. The source is movably mounted relative to the head, and a sensor determines the speed of movement of the head portion across the target area of the patient's skin. The apparatus can include circuitry in communication with the sensor for controlling movement of the source relative to the head portion based on the speed of movement of the head portion across the target area of the patient's skin, such that islets of treatment are formed on the target area of the patient's skin. The circuitry, for instance, can control the movement of the source such that the source is moved in a direction generally opposite the direction of movement of the head portion from a first position in the head portion to a second position in the head portion at generally the same speed as the movement of the head portion, and when the source reaches the second position, it is returned to the first position. The source can, for instance, be mounted on a linear translator in the head portion. In some aspects, the sensor can be a capacitive imaging array or an optical encoder. The source can be either a coherent or a non-coherent light source.

According to another aspect of the invention, an apparatus for performing a treatment on a target area of a patient's skin can prevent the passage of light to the patient's skin if the apparatus is not in contact with the patient's skin. Such an apparatus can feature a light emitting assembly including a non-coherent light source for applying optical energy to the target area and a plurality of light directing elements at an output end of the light emitting assembly. The light directing elements can be shaped so that substantially no light will pass through the output end when the output end is not in contact with the patient's skin. Further, the light directing elements can create treatment islets in the patient's skin during use. The light directing elements can be, for example, selected from a group including an array of pyramids, cones, hemispheres, grooves, and prisms.

According to another aspect of the invention, an apparatus for performing a treatment on a target area of a patient's skin can feature a light emitting assembly

including a non-coherent light source for applying optical energy to the target area, and an element at an output end of the light emitting assembly that includes an optically diffusive surface with optically transmissive spots for output light spatial modulation. The optically transmissive spots can be one or more of circles, slits, rectangles, ovals, or irregular shapes.

Another aspect of the invention is a light emitting assembly for use in performing a treatment on a target area of a patient's skin. According to this aspect, the light emitting assembly includes a non-coherent light source and a light guide for transmitting optical energy from the light source to the target area. The light guide can include a bundle of optical fibers, with the bundle of optical fibers creating islets of treatment on the patient's skin during use. The fibers can be, for instance, spaced apart at an output of the light emitting assembly in order to create the treatment islets. Further, a micro-lens can be attached to an output end of the light guide to focus and/or modulate the light. The light source can be, for example, a linear flash lamp, an arc lamp, an incandescent lamp, or a halogen lamp.

Another aspect of the invention features a light emitting assembly that includes a plurality of non-coherent light sources and a plurality of light guides. Each light guide can transmit optical energy from a different one of the light sources to the target area of the patient's skin. In this aspect, the plurality of light guides provide light spatial modulation. The output ends of the light guides can be used to create islets of treatment on the patient's skin. In this aspect, the light source can be a linear flash lamp, an arc lamp, an incandescent lamp, or a halogen lamp.

Another aspect of the invention is an apparatus for performing a treatment on a target area of a patient's skin that includes a light emitting assembly and a mask. The light emitting assembly is for applying optical energy from an optical energy source to the target area of the patient's skin. The mask is attached to the light emitting assembly, and the mask is positioned between the optical energy source and the target area when the apparatus is in use. The mask includes one or more dielectric layers with a plurality of openings therethrough for passage of optical energy from the optical energy source to the target area. The apparatus can therefore create treatment islets in the patient's skin. In this aspect, the dielectric layers can have a high reflectance over a spectral band emitted

by the optical energy source. The openings in the mask can have various shapes or identical shapes. For instance, the openings can be lines, circles, slits, rectangles, ovals, or irregular shapes. In some aspects, the apparatus can include a cooling or a heating element for cooling or heating the mask during use. The optical energy can be over a wide wavelength band. In one embodiment, infrared light is used. The optical energy can be applied with a pulse width of 100 fsec to 1 sec.

In another aspect, a dermatological device can include a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, a light path between an energy source and the head portion, and a mirror with holes in it. The mirror is within the light path and the holes allow for passage of optical energy from the energy source to the target treatment area. Such a device can be used to create treatment islets in the person's skin. The energy source can be within the device or in a separate unit.

In another aspect of the invention, an apparatus for performing a treatment on a target area of a patient's skin includes a light emitting assembly for applying optical energy to the target area and an element attached to the light emitting assembly. The element is disposed between the light emitting assembly and the target area of the patient's skin when the apparatus is in use, and the element includes a reflective material to reflect optical energy from the light emitting assembly back to the light emitting assembly and openings in the reflective material to allow passage therethrough of optical energy from the light emitting assembly.

According to another aspect of the invention, an apparatus can include a skin lifting implement or vacuum source. According to one aspect, such an apparatus features a skin lifting implement to lift and stretch the target area of the skin beneath the lifting implement and a light emitting assembly for applying optical energy to the target area. During use, the light emitting assembly can be oriented to emit light toward the patient's skin in order to treat the patient's skin. The light emitting assembly can, in one embodiment, create treatment islets in the patient's skin.

Another aspect of the invention is a method for performing a treatment on a target area of a patient's skin beneath a skin fold. According to this aspect, the method includes lifting the patient's skin to form a skin fold and applying light beams from generally

opposite sides of said skin fold such that said light beams intersect at said target area of the patient's skin.

Another aspect of the invention is a composition for use in performing a treatment on a target area of a patient's skin. The composition can feature a material applicable selectively over portions of the target area of a patient's skin. The material can include an absorbing exogenous chromophore. Application of optical energy on the material can selectively heat the portions of the target area. In one aspect, the composition can include a high concentration of the chromophore so that treatment islets are created in the patient's skin. The chromophore can be dispersed within the composition so that only portions of the composition having the chromophore heat up upon the application of the optical energy.

Another aspect of the invention features a substance for use in performing a treatment on a target area of a patient's skin. The substance features a film applicable over the target area of a patient's skin and a composition containing an absorbing exogenous chromophore. The composition is selectively affixed to portions of the film so that application of optical energy on the composition selectively heats the portions of the target area adjacent the composition. The chromophore can be carbon, a metal, an organic dye, a non-organic pigment, or a fullerene. IN one aspect, the composition can be printed using a printing head on the patient's skin. The film can be, for example, an optically clear polymer.

Another aspect of the invention is a kit for use in performing a treatment on a target area of a patient's skin. The kit can include a material applicable selectively over portions of the target area of a patient's skin and a light emitting assembly for applying optical energy to the target area of the patient's skin. The material can include an absorbing exogenous chromophore. In this aspect, application of optical energy from the light emitting assembly on the material heats the exogenous chromophores to selectively heat portions of the target area of the patient's skin. In one aspect, the optical energy has one or more wavelength bands that match the absorption spectrum of the absorbing exogenous chromophore. The material can be, in some aspects, a patch or a lotion for application to the patient's skin.

Another aspect of the invention is a dermatological device that features a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin so that the head portion defines a target treatment area on the person's skin when in contact with the person's skin. The device also includes a substrate having a plurality of absorbing elements, where incident radiation from an energy source heats up the absorbing elements so that the absorbing elements create treatment islets in the stratum corneum of the person's skin. The substrate can be, for instance, a mask that blocks incident radiation in areas of the mask without the absorbing elements. The mask can be a contact plate that acts as a cooling plate in some embodiments. The absorbing elements can be a variety of materials, such as, for example, carbon or a metal.

Another aspect of the invention is a dermatological delivery device. According to this aspect, the device includes a substrate having a plurality of absorbing elements and a composition contained on at least one side of the substrate. Incident radiation from an energy source can heat up the absorbing elements so that the absorbing elements create treatment islets in the stratum corneum of a person's skin. After removal of the substrate, at least a substantial portion of the composition remains on the person's skin.

Another aspect of the invention is a light emitting assembly for use in performing a treatment on a target area of a patient's skin. According to this aspect, the assembly can features a solid state laser, a fiber bundle for receiving optical energy from the laser, and focusing optics at an output end of the fiber bundle for projecting optical energy from each fiber of the fiber bundle onto the target area. The fiber bundle can spatially modulate the optical energy from the laser to create islets of treatment on the patient's skin.

According to another aspect of the invention, a light emitting assembly for use in performing a treatment on a target area of a patient's skin includes a solid state laser, a phase mask including a plurality of openings for propagating emission from the laser, and focusing optics at an output end of the phase mask to provide light spatial modulation on the target area. The light emitting assembly can be used to create islets of treatment on the patient's skin.



Another aspect of the invention includes a light emitting assembly for use in performing a treatment on a target area of a patient's skin. The light emitting assembly can include a bundle of fiber lasers and focusing optics at an output end of the bundle to focus emission of each laser onto the target area. The bundle of fiber lasers and focusing optics can create islets of treatment on the patient's skin.

Another aspect of the invention is an apparatus for performing a treatment on a target area of a patient's skin that includes a light emitting assembly and a plurality of light directing elements. The light emitting assembly includes a light source for applying optical energy to the target area of the patient's skin. The light directing elements are positioned at an output end of the light emitting assembly for output light spatial modulation and concentration. The optical energy can be applied in a multitude of sub-areas, with a substantial portion of the target area between the sub-areas remaining unaffected. The light source is selected from a linear flash lamp, an arc lamp, an incandescent lamp, or a halogen lamp in one embodiment. In other embodiment, the light source can be a solid state laser, a fiber laser, and a dye laser. In one aspect, the light directing elements can be a reflector, a mask, or a light duct. In another aspect, the light directing elements can be a micro lens array, or an array of pyramids, cones, hemispheres, grooves, or prisms. In another aspect, the light direction elements are focusing optics at an output end of a fiber bundle for projecting optical energy from each fiber of the fiber bundle onto the target area.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The following drawings are illustrative of embodiments of the invention and are not meant to limit the scope of the invention as encompassed by the claims.

FIG. 1 is a diagram showing an exemplary cross-section of human skin.

FIG. 2 is a schematic diagram showing the layers of skin.

FIGS. 3A and 3B are semi-schematic perspective and side views respectively of a section of a patient's skin and of equipment positioned thereon for practicing one embodiment.

FIGS. 4A and 4B are top views of various matrix arrays of cylindrical lenses, some of which are suitable for providing a line focus for a plurality of target portions.

FIG. 5 is a side schematic view of some components that can be used in some aspects of the invention.

FIG. 6 is a side view of a hand piece that can be used in some aspects of the invention.

FIG. 7 is a perspective view of another embodiment of the invention.

FIG. 8 is a perspective view of yet another embodiment of the invention.

FIG. 9A is a side view of yet another embodiment of the invention.

FIGS. 9B to 9E are enlarged, side views of the distal end of the embodiment of FIG. 9A.

FIG. 10A is a side view of yet another embodiment of the invention.

FIGS. 10B and 10C are enlarged, side views of the distal end of the embodiment of FIG. 10A.

FIG. 11 is a side view of yet another embodiment of the invention.

FIG. 12A is a side view of an embodiment of the invention using a diode laser bar.

FIG. 12B is a perspective view of a diode laser bar that can be used in the embodiment of FIG. 12A.

FIG. 12C is a side view of yet another embodiment of the invention, which uses multiple diode laser bars.

FIG. 12D is a side view of yet another embodiment of the invention, which uses multiple diode laser bars.

FIG. 12E is a side view of yet another embodiment of the invention, which uses multiple optical fibers to couple optical energy.

FIG. 13A is a side view of another embodiment of the invention.

FIG. 13B is a perspective view of a light source and optical fiber that can be used along with the embodiment of FIG. 13A.

FIG. 13C is a side view of an embodiment of the invention using a fiber bundle.

FIG. 13D is a bottom view of the embodiment of FIG. 13C.

FIG. 13E is an enlarged, side view of a distal end of one of the embodiments of 13A-13D.

FIG. 14A is a side view of another embodiment of the invention, which uses a fiber bundle.

FIG. 14B is a side view of another embodiment of the invention, which uses a phase mask.

FIG. 14C is a side view of another embodiment of the invention, which uses multiple laser rods.

FIG. 15 is a bottom view of another embodiment of the invention, which uses one or more capacitive imaging arrays.

FIG. 16 is a side view of another embodiment of the invention, which uses a motor capable of moving a diode laser bar within a hand piece.

FIG. 17 is a top view of one embodiment of a diode laser bar.

FIG. 18 is a side cross-sectional view of the diode laser bar of FIG. 17.

FIGS. 19A-19C are top views of three optical systems involving arrays of optical elements suitable for use in delivering radiation in parallel to a plurality of target portions.

FIGS. 20A-21D are side views of various lens arrays suitable for delivering radiation in parallel to a plurality of target portions.

FIGS. 22A-22D are side views of Fresnel lens arrays suitable for delivering radiation in parallel to a plurality of target portions.

FIGS. 23A-23C are side views of holographic lens arrays suitable for use in delivering radiation in parallel to a plurality of target portions.

FIGS. 24A-24B are side views of gradient lens arrays suitable for use in delivering radiation in parallel to a plurality of target portions.

FIGS. 25A-25C are top views of various matrix arrays of cylindrical lenses, some of which are suitable for providing a line focus for a plurality of target portions.

FIGS. 26A-26D are cross-sectional or side views of one layer of a matrix cylindrical lens system suitable for delivering radiation in parallel to a plurality of target portions.

FIGS. 27A, 27B, and 27C are a perspective view and cross-sectional side views, respectively, of a two layer cylindrical lens array suitable for delivering radiation in parallel to a plurality of target portions.

FIGS. 28-31 are side views of various optical objective arrays suitable for use in concentrating radiation to one or more target portions.

FIGS. 32A-37 are side views of various deflector systems suitable for use with the arrays of FIGS. 10-13 to move to successive target portions.

FIGS. 38 and 39 are side views of two different variable focus optical system suitable for use in practicing the teachings of this invention.

FIG. 40 is a perspective view of another embodiment of the invention for creating treatment islets.

FIGS. 41A and 41B are side views of yet another embodiment of the invention.

FIGS. 42A and 42B are side and top view, respectively, of an embodiment of the invention having a skin lifting implement, such as a vacuum.

FIG. 43A is a side view of yet another embodiment of the invention.

FIG. 43B is an enlarged, side view of the distal end of the embodiment of FIG. 43A.

FIG. 43C is an enlarged, bottom view of the distal end of the embodiment of FIG. 43A.

FIG. 44 is a perspective view of another embodiment of the invention for creating treatment islets.

FIG. 45 is a perspective shot of two views of another embodiment of the invention for creating treatment islets.

FIG. 46 is a perspective view of another embodiment of the invention for creating treatment islets.

FIG. 47 is a side view of an embodiment of the invention using a film with active islets.

FIG. 48 is a perspective view of another embodiment of the invention for creating treatment islets.

FIGS. 49A to 51B are side views of various embodiments of the invention for creating treatment islets.

FIG. 52-62 are as described in the examples.

FIG. 63 is the four-layer model of skin used in the computational model described in Example 1.

FIG. 64 is the threshold fluence for skin damage at the depths of 0.25 mm (1), 0.5 mm (2), and 0.75 mm (3) in the adiabatic mode as a function of the wavelength.

FIG. 65 is the penetration depth of light inside the type II skin vs. the wavelength for a circular beam of diameter 0.1 mm striking the skin through sapphire.

FIG. 66 is the normalized irradiance on the beam axis as a function of skin depth for 800 (1), 1060 (2), 1200 (3), 1440 (4), 1560 (5), and 1700 (6) nm wavelengths.

FIG. 67 is the normalized irradiance on the beam axis as a function of depth for 1064 nm light focused to skin depths of 0.5 (1), 0.6 (2), 0.7 (3), and 1 (4) mm.

FIG. 68 is tissue irradiance vs. depth for the collimated beam of diameter 10 mm (1) and 0.1 mm (2) striking type II skin surface through sapphire at wavelength 1060 nm.

### DETAILED DESCRIPTION

The present invention depends, in part, upon the discovery that, when using electromagnetic radiation (EMR) to treat tissues, whether for purposes of photodynamic therapy, photobleaching, photobiomodulation, photobiostimulation, photobiosuspension, thermal stimulation, thermal coagulation, thermal ablation or other applications, there are substantial advantages to producing lattices of EMR-treated islets in the tissue rather than large, continuous regions of EMR-treated tissue. The EMR-treated tissues can be any tissues for which such treatment is useful and appropriate, including but not limited to dermal tissues, mucosal tissues (*e.g.*, oral mucosa, gastrointestinal mucosa), ophthalmic tissues (*e.g.*, retinal tissues), vaginal tissue and glandular tissues (*e.g.*, prostate tissue).

The lattices are periodic patterns of islets in one, two or three dimensions in which the islets correspond to local maxima of EMR-treatment of tissue. The islets are separated from each other by non-treated tissue (or differently- or less-treated tissue). The EMR-treatment results in a lattice of EMR-treated islets which have been exposed to a particular wavelength or spectrum of EMR, and which is referred to herein as a lattice of "optical islets." When the absorption of EMR energy results in significant temperature elevation in the EMR-treated islets, the lattice is referred to herein as a lattice of "thermal islets." When an amount of energy is absorbed that is sufficient to significantly disrupt cellular or intercellular structures, the lattice is referred to herein as a lattice of "damage islets." When an amount of energy (usually at a particular wavelength) sufficient to

initiate a certain photochemical reaction is delivered, the lattice is referred to herein as a lattice of "photochemical islets."

By producing EMR-treated islets rather than continuous regions of EMR-treatment, untreated regions (or differently- or less-treated regions) surrounding the islets can act as thermal energy sinks, reducing the elevation of temperature within the EMR-treated islets and/or allowing more EMR energy to be delivered to an islet without producing a thermal islet or damage islet and/or lowering the risk of bulk tissue damage. Moreover, with respect to damage islets, it should be noted that the regenerative and repair responses of the body occur at wound margins (*i.e.*, the boundary surfaces between damaged and intact areas) and, therefore, healing of damaged tissues is more effective with smaller damage islets, for which the ratio of the wound margin to volume is greater.

As described more fully below, the percentage of tissue volume which is EMR-treated versus untreated (or differently- or less-treated) can determine whether optical islets become thermal islets, damage islets or photochemical islets. This percentage is referred to as the "fill factor", and can be decreased by increasing the center-to-center distance(s) of islets of fixed volume(s), and/or decreasing the volume(s) of islets of fixed center-to-center distance(s).

Because untreated tissue volumes act as a thermal sink, these volumes can absorb energy from treated volumes without themselves becoming thermal or damage islets. Thus, a relatively low fill factor can allow for the delivery of high fluence energy to some volumes while preventing the development of bulk tissue damage. Finally, because the untreated tissue volumes act as a thermal sink, as the fill factor decreases, the likelihood of optical islets reaching critical temperatures to produce thermal islets or damage islets also decreases (even if the EMR power density and total exposure remain constant for the islet areas).

Finally, as described in detail below, the present invention also depends, in part, upon the application of discoveries relating to the EMR and thermal energy absorption, transfer, and dissipation properties of tissue. Based, in part, upon these discoveries, the invention provides improved devices and systems for producing lattices of EMR-treated islets in tissues, and improved cosmetic and medical applications of such devices and systems in dermatology, dentistry, ophthalmology, gynecology, otorhinolaryngology and

internal medicine in combination with endoscope and catheter techniques. Although the devices, systems and methods of the invention are described in detail for dermatological applications, they can be used for treatment of any tissue surface or subsurface areas to which EMR can be delivered.

#### References and Definitions.

The patent, scientific and medical publications referred to herein establish knowledge that was available to those of ordinary skill in the art at the time the invention was made. The entire disclosures of the issued U.S. patents, published and pending patent applications, and other references cited herein are hereby incorporated by reference.

All technical and scientific terms used herein, unless otherwise defined below, are intended to have the same meaning as commonly understood by one of ordinary skill in the art. References to techniques employed herein are intended to refer to the techniques as commonly understood in the art, including variations on those techniques or substitutions of equivalent or later-developed techniques which would be apparent to one of skill in the art. In addition, in order to more clearly and concisely describe the subject matter which is the invention, the following definitions are provided for certain terms which are used in the specification and appended claims.

Numerical Ranges. As used herein, the recitation of a numerical range for a variable is intended to convey that the invention may be practiced with the variable equal to any of the values within that range. Thus, for a variable which is inherently discrete, the variable can be equal to any integer value within the numerical range, including the end-points of the range. Similarly, for a variable which is inherently continuous, the variable can be equal to any real value within the numerical range, including the end-points of the range. As an example, and without limitation, a variable which is described as having values between 0 and 2 can take the values 0, 1 or 2 if the variable is inherently discrete, and can take the values 0.0, 0.1, 0.01, 0.001, or any other real values  $\geq 0$  and  $\leq 2$  if the variable is inherently continuous. Finally, the variable can take multiple values in the range, including any sub-range of values within the cited range.

Or. As used herein, unless specifically indicated otherwise, the word "or" is used in the inclusive sense of "and/or" and not the exclusive sense of "either/or."

### Skin Structure

Although the devices and systems of the invention, and the general methods of the invention, can be practiced with many tissues of the body, currently the most common applications of EMR-treatment to tissues are in the field of dermatology. Therefore, the structure of the skin, including its constituent tissues, is described below in some detail, and the remainder of the disclosure will use the skin as an example. In addition, certain applications will be described which are uniquely adapted to the skin (*e.g.*, tattoo removal, permeation of the stratum corneum). It should be understood, however, that the general methods are applicable to other tissues, and that one of ordinary skill in the art can adapt the teachings of the disclosure to other organs and tissues with merely routine experimentation.

The skin is the largest organ in the human body, consisting of several layers of distinct tissues with distinct properties, and ranges in thickness from approximately 0.5 mm to approximately 4 mm. Fig. 1 illustrates a typical cross section of skin 150, showing various layers with differing cellular and intercellular structures.

The skin lies on top of the superficial fascia or subcutaneous tissue 160, a layer of fatty tissue that overlies the more densely fibrous fascia.

Above the subcutaneous tissue is the dermis 170, which comprises fibroelastic connective tissue, and ranges in thickness from approximately 0.3 mm on the eyelids to approximately 3.0 mm on the back. The dermis is highly vascularized and includes a variety of sensory nerves with temperature, pressure and pain receptors that are organized into small nerve bundles that ascend along with the blood vessels and lymphatic vessels to form a network of interlacing nerves beneath the epidermis, *i.e.*, the superficial nerve plexus of the papillary dermis. Some of the nerves appear to penetrate the epidermis for short distances. The dermis includes two layers: a reticular layer 171 and a papillary layer 172. The reticular layer 171 includes cells in a matrix of dense, coarse bundles of collagenous fibers. The papillary layer 172 includes cells in a matrix of loose



collagenous and elastic fibers, with elevations or papillae which project toward the epidermis. Cell types in the dermis include fibroblasts, mast cells and macrophages.

The epidermis 180 comprises the outermost stratified layers of the skin, and ranges in thickness from approximately 0.05 mm on the eyelids to approximately 1.5 mm on the palms and soles. The epidermis is avascular and consists largely of epithelial cells which mature as they pass from the innermost layer of columnar cells to the outermost layer of tile-like squamous cells, with the cells becoming increasingly flattened and keratinized as they progress outward. The innermost layer is referred to as the stratum basale, basal cell layer, or stratum germinativum 181, and is the only layer in normal epidermis in which cell division occurs. The next layer, the stratum spinosum 182, includes prickle cells and keratinocytes, and begins the production of keratin. The next layer, the stratum granulosum 183, is a darker layer with intercellular granules and increased keratin production. In thick skin, there is an additional transitional layer, the stratum lucidum 184. Finally, the outermost layer is the stratum corneum (SC) 185, a horny layer of highly keratinized squamous cells.

The cells of the stratum corneum 185 (and the stratum lucidum 184, when present) are highly keratinized ("horny") and surrounded by an extracellular matrix consisting largely of crystalline lipids. As a result, the stratum corneum forms a hard, resilient barrier to water transport, and is not permeable to most aqueous or organic solvents or solutes. The stratum corneum 185 is about 15  $\mu\text{m}$  deep on most anatomic sites but can be in the ranges of 10-300  $\mu\text{m}$  (e.g., 20  $\mu\text{m}$  at the forearm and 50-60  $\mu\text{m}$  at the wrist).

Also shown are typical organs and structures within the skin, including a hair follicle 190, blood vessels 191, nerve fibers 192, a sweat gland 193, a sebaceous gland 194, and an arrector pili muscle 195.

Normal skin temperature is approximately 29-37°C. When exposed to temperatures in excess of 40-43°C, the sensory nerves of the dermis will transmit a pain response in most human subjects.

Fig. 2 is a schematic cross-sectional view of a human skin section 150. It shows depths into the skin, from the surface in  $\mu\text{m}$ . The stratum corneum 185 and stratum lucidum 184 are shown extending to a depth of approximately 15  $\mu\text{m}$  below the skin

surface. The remaining layers (*i.e.*, layers 181-183) of the epidermis 180 extend from the stratum lucidum/corneum 184/185 to the boundary with the dermis 170 at a depth from the surface in the range of approximately 50-150  $\mu\text{m}$ . Also shown are exemplary shallow islets 196 affecting the stratum lucidum/corneum 184/185, deeper islets 197 affecting the stratum lucidum/corneum 184/185 and deeper layers of the epidermis 180, and subsurface islets 198 spanning portions of the deeper epidermis 180 and upper dermis 170.

The depths shown in Fig. 2 are merely exemplary. Different locations in the typical human body have different depth profiles for the stratum corneum/lucidum, epidermis, and dermis. In addition, as described below, a great variety of other islet configurations are possible which are not shown in the figure (*e.g.*, islets entirely in the dermis; islets entirely in the subcutaneous tissue; islets spanning the dermis and subcutaneous tissue; islets spanning portions of the epidermis, dermis and subcutaneous tissue).

#### Categories of EMR-Treated Islets

The present invention depends, in part, on the creation of a multiplicity of treated volumes of the skin which are separated by untreated volumes. The multiplicity of volumes can be described as defining a "lattice," and the treated volumes, because they are separated by untreated volumes, can be described as "islets" within the skin. Depending upon the nature of the treatment, in particular the amount of energy transfer to the islets, the degree of heating of the tissue, or the wavelength(s) of the energy, four different categories of lattices can be produced: lattices of optical islets (LOI), lattices of thermal islets (LTI), lattices of damage islets (LDI), and lattices of photochemical islets (LPCI). These different categories of EMR-treated islets, devices and systems for producing such EMR-treated islets, and cosmetic and medical applications for such devices and systems are separately discussed in detail below. As used herein, the terms "treatment islet," "islets of treatment," and "EMR-treated islets" are used interchangeably to mean any of the categories of islets described below.

### A. Optical Islets

In accordance with the present invention, EMR-treatment of completely or partially isolated volumes or islets of tissue produces a lattice of EMR-treated islets surrounded by untreated volumes. Although the islets can be treated with any form of EMR, they are referred to herein as "optical" islets for convenience, as many embodiments of the invention include the use of EMR within the ultraviolet, visible and infra-red spectrum. Other forms of EMR useful in the invention include microwave, radio frequency, low frequency and EMR induced by direct current.

As noted above, when the total energy transfer per unit cross-sectional area (*i.e.*, fluence) or the rate of energy transfer per unit cross-sectional area (*i.e.*, flux) becomes sufficiently high, the tissue of an optical islet will be heated, resulting in a thermal islet. If the temperature increase is sufficiently high, the tissue of a thermal islet will be damaged, resulting in a damage islet. Thus, although all thermal islets and damage islets are also optical islets, not all optical islets are thermal islets or damage islets. In some embodiments, as described below, it can be desirable to produce optical islets without producing thermal or damage islets. In such embodiments, the fill factor can be decreased in order to provide a greater volume of untreated tissue to act as a thermal sink.

As described in detail in the Examples below, a model of optical islets was developed which describes the propagation of light into skin taking into account the skin type and the characteristics of the light source. The particular approach used below is applicable to a wide range of islet dimensions (*e.g.*, 10-30,000  $\mu\text{m}$  in the lateral plane), is generally accepted in tissue optics, and is referred to as the light transport theory (Chandrasekhar (1960), Radiative Transfer (University Press, Oxford); Ishimaru (1978), Wave Propagation and Scattering in Random Media, Volume 1 (Academic Press, New York); Jacques *et al.* (1995), in Optical-Thermal Response of Laser-Irradiated Tissue, Welch *et al.*, eds. (Plenum Press, New York), pp. 561-606). Briefly, the skin is considered as a multilayer structure with each layer being a turbid medium where light undergoes both absorption and multiple scattering. This approach neglects macroscopic coherence effects like diffraction and speckle formation. Several techniques may be used to solve the light transport problem in a tissue. Some of them, particularly the two-flux and diffusion approximations, break down when the input beam is sufficiently narrow or

is focused into the tissue, and are not suitable for dealing with the islet formation problem. The Monte-Carlo technique described below is not subject to such limitations and is capable of modeling various tissue structures, spot profiles, wavelength spectra, and angular distributions of the incident light (Jacques *et al.* (1995), *supra*).

### B. Thermal Islets

In accordance with another aspect of the present invention, EMR-treatment of isolated volumes or islets of tissue can produce a lattice of thermal islets with temperatures elevated relative to those of surrounding untreated volumes. Thermal islets result when energy is absorbed by an EMR-treated optical islet significantly faster than it is dissipated and, therefore, significant heating occurs.

Heating can result from the absorbance of EMR by water present throughout a volume of treated tissue, by endogenous chromophores present in selected cells or tissue(s) (*e.g.*, melanin, hemoglobin), by exogenous chromophores within the tissue (*e.g.*, tattoo ink) or, as described below, by exogenous chromophores applied to the surface of the tissue.

With respect to skin, in order to avoid causing pain to a subject, the maximal temperature of the basal membrane, which is adjacent to the nerve terminals of the papillary dermis, should not exceed 40-45°C. Assuming no active cooling of the skin surface, the temperature rise in the basal membrane,  $\Delta T_2$ , can be related to the temperature rise in the hyperthermic islets,  $\Delta T_1$ , by an approximate formula:

$$\Delta T_2 = f \Delta T_1$$

where  $f$  is the fill-factor of the optical lattice at the skin surface. This formula indicates that the temperature in the SC can attain relatively high values without triggering the pain response of the body if the fill factor is sufficiently low.

For example, setting  $\Delta T_2$  to 12°C and  $f$  to 0.3 yields  $\Delta T_1$  of 40°C. In practice, the temperature rise  $\Delta T_1$  may be limited by other factors, such as, for example, the threshold of structural damage to the SC or the desired size of the damage islets.

The thermal islet model is based, in part, on the time-dependent heat equation. Specifically, as described in more detail below, the thermal constants of the skin layers

are obtained from Takata's relations (Takata *et al.* (1977), in *Report SAM-TR-77-38* (San Antonio, TX: US Air Force School for Aerospace Medicine)) and are functions of the volume fraction of water in the corresponding layer. Specific effects associated with the bio-heat equation, *e.g.*, the metabolic heat generation and the change of the blood perfusion rate while heating the living tissue, can be neglected for EMR pulses of short duration (Sekins *et al.* (1990), *Thermal Science for Physical Medicine*, in *Therapeutic Heat and Cold*, 4th edition, Lehmann, ed. (Baltimore: Williams & Wilkins) pp. 62-112). In practice, the EMR-heating can dominate strongly over metabolic heating and heat transfer by the blood flow. Moreover, the changes in the blood perfusion rate can occur with the delay of about 1 min with respect to the variations of the tissue temperature (Sekins *et al.* (1990), in *Therapeutic Heat and Cold*, 4th edition, Lehmann, ed. (Baltimore: Williams & Wilkins) pp. 62-112), and do not affect the islet formation dynamics unless tissues are under combined action (with EMR) of simultaneous physical factors (*e.g.*, elevated or lowered external pressure, ultrasound, elevated or lowered skin surface temperature).

It should be emphasized that a lattice of thermal islets is a time-dependent phenomenon. If absorptive heating occurs at too great a rate or for too long a period, heat will begin to diffuse away from the EMR-treated islets and into the surrounding untreated tissue volumes. As this occurs, the thermal islets will spread into the untreated volumes and, ultimately, the thermal islets will merge and result in bulk heating. By using a sufficiently short pulse width relative to the temperature relaxation time of the target, it is possible to avoid merging or overlapping of thermal islets in a lattice.

### C. Damage Islets

In accordance with another aspect of the present invention, EMR-treatment of isolated volumes or islets of tissue can produce a lattice of damage islets surrounded by volumes of undamaged tissue (or differently- or less-damaged tissue). Damage islets result when the temperature increase of an EMR-treated thermal islet is sufficient to result in protein coagulation, thermal injury, photodisruption, photoablation, or water vaporization. Depending upon the intended use, damage islets with lesser degrees of damage (*e.g.*, protein coagulation, thermal injury) or greater degrees of damage (*e.g.*, photodisruption, photoablation, or water vaporization) may be appropriate. As before,

damage can result from the absorbance of EMR by water present throughout a volume of treated skin, by endogenous chromophores present in selected cells or tissue(s) in the skin (*e.g.*, melanin, hemoglobin), by exogenous chromophores within the skin (*e.g.*, tattoo ink) or, as described below, by exogenous chromophores applied to the surface of the skin.

As described in detail below, in some embodiments of the invention, the damage islets are thermal injuries with coagulation of structural proteins. Such damage can result when, for example, the light pulse duration varies from several microseconds to about 1 sec, but the peak tissue temperature remains below the vaporization threshold of water in the tissue (Pearce *et al.* (1995), in Optical-Thermal Response of Laser-Irradiated Tissue, Welch *et al.*, eds. (Plenum Press, New York), pp. 561-606). The degree of damage is a function of the tissue temperature and the duration of the thermal pulse, and can be quantified by any of several damage functions known in the art. In the description below, for example, the damage function yielding the Arrhenius damage integral (Pearce *et al.* (1995), in Optical-Thermal Response of Laser-Irradiated Tissue, Welch *et al.*, eds. (Plenum Press, New York), pp. 561-606; Henriques (1947), *Arch. Pathol.* 43:480-502) is employed. Other mechanisms and models of damage islet formation can apply to embodiments with relatively short and intense pulses, particularly in connection with photodisruption, photoablation, and water vaporization.

#### D. Photochemical Islets

In accordance with another aspect of the present invention, EMR-treatment of isolated volumes or islets of tissue can produce a lattice of photochemical islets surrounded by volumes of tissue in which a photochemical reaction has not been induced. The photochemical reaction can involve endogenous biomolecules or exogenous molecules. For example, exposure of the skin to certain wavelengths of EMR can result in increased melanin production and "tanning" through the activation of endogenous biomolecules and biological pathways. Alternatively, for example, exogenous molecules can be administered in photodynamic therapy, and activation of these molecules by certain wavelengths of EMR can cause a systemic or localized therapeutic effect.

Treatment Parameters.

In the practice of the invention, a variety of different treatment parameters relating to the applied EMR can be controlled and varied according to the particular cosmetic or medical application. These parameters include, without limitation, the following:

A. The Shape of EMR-Treated Islets.

The optical islets can be formed in any shape which can be produced by the devices described below, limited only by the ability to control EMR beams within the tissue. Thus, depending upon the wavelength(s), temporal characteristics (*e.g.*, continuous versus pulsed delivery), and fluence of the EMR; the geometry, incidence and focusing of the EMR beam; and the index of refraction, absorption coefficient, scattering coefficient, anisotropy factor (the mean cosine of the scattering angle), and the configuration of the tissue layers; and the presence or absence of exogenous chromophores and other substances, the islets can be variously-shaped volumes extending from the surface of the skin through one or more layers, or extending from beneath the surface of the skin through one or more layers, or within a single layer. If the beams are not convergent, such beams will define volumes of substantially constant cross-sectional areas in the plane orthogonal to the beam axis (*e.g.*, cylinders, rectanguloids). Alternatively, the beams can be convergent, defining volumes of decreasing cross-sectional area in the plane orthogonal to the central axis of the beams (*e.g.*, cones, pyramids). The cross-sectional areas can be regular in shape (*e.g.*, ellipses, polygons) or can be arbitrary in shape. In addition, depending upon the wavelength(s) and fluence of an EMR beam, and the absorption and scattering characteristics of a tissue for the wavelength(s), an EMR beam may penetrate to certain depths before being initially or completely absorbed or dissipated and, therefore, an EMR-treated islet may not extend through the entire depth of the skin but, rather, may extend between the surface and a particular depth, or between two depths below the surface.

Generally, the lattice is a periodic structure of islets in one, two, or three dimensions. For instance, a two-dimensional (2D) lattice is periodic in two dimensions and translation invariant or non-periodic in the third. The type of periodicity is characterized by the voxel shape. For example, and without limitation, there can be

layer, square, hexagonal or rectangle lattices. The lattice dimensionality can be different from that of an individual islet. A single row of equally spaced infinite cylinders is an example of the 1D lattice of 2D islets (if the cylinders are of finite length this is the 1D lattice of 3D islets). The lattice dimensionality is equal to or smaller than the dimensionality of its islets (this fact follows from the fact that the lattice cannot be periodic in the dimension where its islets are translation invariant). Hence, there exists a total of 6 lattice types with each type being an allowed combination of the islet and lattice dimensionalities. For certain applications, an "inverted" lattice can be employed, in which islets of intact tissue are separated by areas of EMR-treated tissue and the treatment area is a continuous cluster of treated tissue with non treated islands.

Referring to Figure 3A, each of the treated volumes can be a relatively thin disk, as shown, a relatively elongated cylinder (*e.g.*, extending from a first depth to a second depth), or a substantially linear volume having a length which substantially exceeds its width and depth, and which is oriented substantially parallel to the skin surface. The orientation of the lines for the islets 214 in a given application need not all be the same, and some of the lines may, for example, be at right angles to other lines (see for example Figs. 4A and 4B). Lines also can be oriented around a treatment target for greater efficacy. For example, the lines can be perpendicular to a vessel or parallel to a wrinkle. Islets 214 can be subsurface volumes, such as spheres, ellipsoids, cubes or rectangularoids of selected thickness. The islets can also be substantially linear or planar volumes. The shapes of the islets are determined by the combined optical parameters of the beam, including beam size, amplitude and phase distribution, the duration of application and, to a lesser extent, the wavelength.

The parameters for obtaining a particular islet shape can be determined empirically with only routine experimentation. For example, a 1720 nm laser operating with a low conversion beam at approximately 0.005-2 J and a pulse width of 0.5-2 ms, can produce a generally cylindrically shaped islet. Alternatively, a 1200 nm laser operating with a highly converting beam at approximately 0.5-10 J and a pulse width of 0.5-3 sec, can produce a generally ellipsoid-shaped islet.

By suitable control of wavelength, focusing, incident beam size at the surface and other parameters, the islets, regardless of shape, can extend through a volume, can be



formed in a single thin layer of a volume, or can be staggered such that adjacent islets are in different thin layers of volume. Most configurations of a lattice of islets can be formed either serially or in simultaneously. Lattices with islets in multiple thin layers in a volume can be easily formed serially, for example using a scanner or using multiple energy sources having different wavelengths. Islets in the same or varying depths can be created, and when viewed from the skin surface, the islets at varying depths can be either spatially separated or overlapping.

The geometry of the islets affects the thermal damage in the treatment region. Since a sphere provides the greatest gradient, and is thus the most spatially confined, it provides the most localized biological damage, and can therefore be preferred for applications where this is desirable.

#### B. The Size of EMR-Treated Islets.

The size of the individual islets within the lattices of EMR-treated islets of the invention, can vary widely depending upon the intended cosmetic or medical application. As discussed more fully below, in some embodiments it is desirable to cause substantial tissue damage to destroy a structure or region of tissue (*e.g.*, a sebaceous gland, hair follicle, tattooed area) whereas in other embodiments it is desirable to cause little or no damage while administering an effective amount of EMR at a specified wavelength (*e.g.*, photodynamic therapy). As noted above with respect to damage islets, however, the healing of damaged tissues is more effective with smaller damage islets, for which the ratio of the wound margin to volume is greater.

As a general matter, the size of the EMR-treated islets of the present invention can range from 1  $\mu\text{m}$  to 30 mm in any particular dimension. For example, and without limitation, a lattice of substantially linear islets can consist of parallel islets have a length of approximately 30 mm and a width of approximately 10  $\mu\text{m}$  to 1 mm. As another example, and without limitation, for substantially cylindrical islets in which the axis of the cylinder is orthogonal to the tissue surface, the depth can be approximately 10  $\mu\text{m}$  to 4 mm and the diameter can be approximately 10  $\mu\text{m}$  to 1 mm. For substantially spherical or ellipsoidal islets, the diameter or major axis can be, for example, and without limitation, approximately 10  $\mu\text{m}$  to 1 mm. Thus, in some embodiments, the islets can have a maximum dimension in the range from 1  $\mu\text{m}$  to 10  $\mu\text{m}$ , 10  $\mu\text{m}$  to 100  $\mu\text{m}$ , 100  $\mu\text{m}$

to 1 mm, 1 mm to 10 mm, or 10 mm to 30 mm, as well as all possible ranges within 1  $\mu\text{m}$  to 30 mm.

When considering the size of the optical, thermal, damage or photochemical islets of the invention, it is important to note that the boundaries of the islets may not be clearly demarcated but, rather, may vary continuously or blend into the untreated tissue (or differently- or less-treated tissue). For example, EMR beams are subject to scattering in various tissues and, therefore, even beams of coherent light will become diffuse as they penetrate through multiple layers of cells or tissues. As a result, optical and photochemical islets typically will not have clear boundaries between treated and untreated volumes. Similarly, thermal islets typically will exhibit a temperature gradient from the center of the islet to its boundaries, and untreated tissue surrounding the islet also will exhibit a temperature gradient due to conduction of heat. Finally, damage islets can have irregular or indistinct boundaries due to partially damaged cells or structures or partially coagulated proteins. As used herein, therefore, the size of an islet within a lattice of islets, refers to the size of the islet as defined by the intended minimum or threshold amount of EMR energy delivered. As discussed in greater detail below, this amount is expressed as the minimum fluence,  $F_{\text{min}}$ , and is determined by the nature of the cosmetic or medical application. For example, for photodynamic therapy,  $F_{\text{min}}$  can be determined by the minimum fluence necessary to cause the desired photochemical reaction. Similarly, for increasing the permeability of the stratum corneum,  $F_{\text{min}}$  can be determined by the minimum fluence necessary to achieve the desired SC temperature, and for destroying tissue,  $F_{\text{min}}$  can be determined by the minimum fluence necessary to ablate the tissue or vaporize water. In each case, the size of the EMR-treated islet is defined by the size of the tissue volume receiving the desired minimum fluence.

Because of the scattering effects of tissue, the minimum size of an EMR-treated islet increases with the targeted depth in the tissue, ranging from several microns on the stratum corneum to several millimeters in subcutaneous tissue. For a depth of approximately 1 mm into a subject's tissue, the minimum diameter or width of an islet is estimated to be approximately 100  $\mu\text{m}$ , although much larger islets (*e.g.*, 1-10 mm) are possible. The size of a damage islet can be either smaller or larger than the size of the corresponding optical islet, but is generally larger as greater amounts of EMR energy are

applied to the optical islet due to heat diffusion. For a minimum size islet at any particular depth in the skin, the wavelength, beam size, convergence, energy and pulse width have to be optimized.

#### C. The Depth of EMR-Treated Islets.

The EMR-treated islets of the invention can be located at varying points within a tissue, including surface and subsurface locations, locations at relatively limited depths, and locations spanning substantial depths. The desired depth of the islets depends upon the intended cosmetic or medical application, including the location of the targeted molecules, cells, tissues or intercellular structures.

For example, optical islets can be induced at varying depths in a tissue or organ, depending upon the depth of penetration of the EMR energy, which depends in part upon the wavelength(s) and beam size. Thus, the islets can be shallow islets that penetrate only surface layers of a tissue (*e.g.*, 0-50  $\mu\text{m}$ ), deeper islets that span several layers of a tissue (*e.g.*, 50-500  $\mu\text{m}$ ), or very deep, subsurface islets (*e.g.*, 500  $\mu\text{m}$  - 4 mm). Using optical energy, depths of up to 25 mm can be achieved using wavelengths of 1,000-1,300 nm. Using microwave and radio frequency EMR, depths of several centimeters can be achieved.

For thermal islets or damage islets, subsurface islets can be produced by targeting chromophores present only at the desired depth(s), or by cooling upper layers of a tissue while delivering EMR. For creating deep thermal or damage islets, long pulse widths coupled with surface cooling can be particularly effective.

#### D. Fill Factor of EMR-Treated Lattices

In a given lattice of EMR-treated islets, the percentage of tissue volume which is EMR-treated is referred to as the "fill factor" or *f*, and can affect whether optical islets become thermal islets, damage islets or photochemical islets. The fill factor is defined by the volume of the islets with respect to a reference volume that contains all of the islets. The fill factor may be uniform for a periodic lattice of uniformly sized EMR-treated islets, or it may vary over the treatment area. Non-uniform fill factors can be created in situations including, but not limited to, the creation of thermal islets using topical application of EMR-absorbing particles in a lotion or suspension (see below). For such

situations, an average fill factor ( $f_{avg}$ ) can be calculated by dividing the volume of all EMR-treated islets  $V_i^{islet}$  by the volume of all tissue  $V_i^{tissue}$  in the treatment area,

$$f_{avg} = \sum_i \frac{V_i^{islet}}{V_i^{tissue}}.$$

Generally, the fill factor can be decreased by increasing the center-to-center distance(s) of islets of fixed volume(s), and/or decreasing the volume(s) of islets of fixed center-to-center distance(s). Thus, the calculation of the fill factor will depend on volume of an EMR-treated islet as well as on the spacing between the islets. In a periodic lattice, where the centers of the nearest islets are separated by a distance  $d$ , the fill factor will depend on the ratio of the size of the islet to the spacing between the nearest islets  $d$ . For example, in a lattice of parallel cylindrical islets, the fill factor will be:

$$f = \pi \left( \frac{r}{d} \right)^2,$$

where  $d$  is the shortest distance between the centers of the nearest islets and  $r$  is the radius of a cylindrical EMR-treated islet. In a lattice of spherical islets, the fill factor will be the ratio of the volume of the spherical islet to the volume of the cube defined by the neighboring centers of the islets:

$$f = \frac{4\pi}{3} \left( \frac{r}{d} \right)^3,$$

where  $d$  is the shortest distance between the centers of the nearest islets and  $r$  is the radius of a spherical EMR-treated islet. Similar formulas can be obtained to calculate fill factors of lattices of islets of different shapes, such as lines, disks, ellipsoids, rectanguloids, or other shapes.

Because untreated tissue volumes act as a thermal sink, these volumes can absorb energy from treated volumes without themselves becoming thermal or damage islets. Thus, a relatively low fill factor can allow for the delivery of high fluence energy to some volumes while preventing the development of bulk tissue damage. Finally, because the untreated tissue volumes act as a thermal sink, as the fill factor decreases, the likelihood of optical islets reaching critical temperatures to produce thermal islets or damage islets

also decreases (even if the EMR power density and total exposure remain constant for the islet areas).

The center-to-center spacing of islets is determined by a number of factors, including the size of the islets and the treatment being performed. Generally, it is desired that the spacing between adjacent islets be sufficient to protect the tissues and facilitate the healing of any damage thereto, while still permitting the desired therapeutic effect to be achieved. In general, the fill factor can vary in the range of 0.1-90%, with ranges of 0.1-1%, 1-10%, 10-30% and 30-50% for different applications. The interaction between the fill factor and the thermal relaxation time of a lattice of EMR-treated islets is discussed in detail below. In the case of lattices of thermal islets, it can be important that the fill factor be sufficiently low to prevent excessive heating and damage to islets, whereas with damage islets it can be important that the fill factor be sufficiently low to ensure that there is undamaged tissue around each of the damage islets sufficient to prevent bulk tissue damage and to permit the damaged volumes to heal.

#### Applications of EMR-Treated Islets

EMR-treated islets can be used in a variety of applications in a variety of different organs and tissues. For example, EMR treatments can be applied to tissues including, but not limited to, skin, mucosal tissues (*e.g.*, oral mucosa, gastrointestinal mucosa), ophthalmic tissues (*e.g.*, conjunctiva, cornea, retina), and glandular tissues (*e.g.*, lacrimal, prostate glands). As a general matter, the methods can be used to treat conditions including, but not limited to, lesions (*e.g.*, sores, ulcers), acne, rosacea, undesired hair, undesired blood vessels, hyperplastic growths (*e.g.*, tumors, polyps, benign prostatic hyperplasia), hypertrophic growths (*e.g.*, benign prostatic hypertrophy), neovascularization (*e.g.*, tumor-associated angiogenesis), arterial or venous malformations (*e.g.*, hemangiomas, nevus flammeus), and undesired pigmentation (*e.g.*, pigmented birthmarks, tattoos).

#### A. Thermal Islets

In some aspects, the invention provides methods of treating tissues by creating lattices of thermal islets. These methods can be used in, for example, methods of

increasing the permeability of the stratum corneum to various agents, including therapeutic agents and cosmetic agents, and methods for producing therapeutic hyperthermia.

#### 1. Reversible Permeation of the Stratum Corneum

In one embodiment, lattices of thermal islets are produced in order to reversibly increase the permeability of the stratum corneum by heating islets of tissue to temperatures of 35-100°C. The increased permeability results from the melting of the extracellular matrix of crystalline lipids that surrounds the cells of the stratum corneum and, when present, the stratum lucidum. When this matrix melts (*i.e.*, loses its crystalline structure), the SC becomes more permeable to molecules on the surface of the skin, allowing some molecules to diffuse inward. When the temperature of the layer returns to the normal range (*i.e.*, 29-37°C), the intercellular matrix recrystallizes, the SC becomes more impermeable, and any molecules which had diffused below the SC can remain there, further diffuse into surrounding tissues, or enter the systemic circulation. Thus, as used herein, the increased permeability is "reversible" because the lipid intercellular matrix recrystallizes. In different embodiments, the increase in permeability is reversed within 1 second to 2 hours after the EMR-treatment is discontinued. Thus, in some embodiments, the increase in permeability is reversed within 15 minutes, 30 minutes, 1 hour or 2 hours after the EMR-treatment is discontinued.

In these embodiments, the thermal islets define permeation pathways which can extend through or mostly through the stratum corneum and stratum lucidum layers so that a compound, for example, a cosmetic or therapeutic agent applied to the exterior surface of the skin is able to efficiently penetrate the stratum corneum/stratum lucidum. This penetration can be superficial and remain just below or within the stratum corneum, or can be deeper into the interior layers of the epidermis or dermis and, possibly, into the blood stream via the vascularization in the dermis. This enables the percutaneous delivery of cosmetic or therapeutic agents locally to the epidermis and dermis. To the extent the compound diffuses away from the site of treatment, the local delivery of the compound can be greater (*e.g.*, delivery to a joint region). Moreover, to the extent that the compound reaches the vasculature of the dermis, delivery can be systemic.

In some embodiments, the compound is a therapeutic agent. Examples of therapeutic agents include, without limitation, a hormone, a steroid, a non-steroidal anti-inflammatory drug, an anti-neoplastic agent, an antihistamine and an anesthetic agent. Specific examples include, without limitation, hormones such as insulin and estrogen, steroids such as prednisolone and loteprednol, non-steroidal anti-inflammatory drugs such as ketorolac and diclofenac, anti-neoplastic agents such as methotrexate, and antihistamines such as histamine H1 antagonists, chlorpheniramine, pyrilamine, mepyramine, emedastine, levocabastine and lidocaine.

In other embodiments, the compound is a cosmetic agent. Examples of cosmetic agents include, without limitation, pigments (including both naturally occurring and synthetic chromophores, dyes, colorants or inks) reflective agents (including light-scattering compounds), and photoprotectants (including sunscreens). Such cosmetic agents can be used to add coloration to the skin, or to mask existing coloration (*e.g.*, birthmarks, pigmented lesions, tattoos) by adding differently colored pigments or reflective agents. The invention provides improved methods of applying cosmetic agents because (a) the agents are contained within the stratum corneum and will not be smeared, or rubbed or washed off, and (b) the agents will remain within the stratum corneum until the cells of that layer are replaced through the normal process of outgrowth from the stratum basale (*e.g.*, approximately 21-28 days). Thus, a single application of a cosmetic agent can last for several weeks, which can be advantageous relative to cosmetics which must be applied daily. Conversely, the application of the cosmetic agent is limited to several weeks, which can be advantageous relative to tattoos which are usually permanent unless removed by photobleaching or tissue ablation. In one embodiment, pigments for a desired temporary tattoo can be applied to the skin (*e.g.*, by a film, brush, printing), the stratum corneum can be EMR-treated to increase permeability, and the pigments can diffuse into the skin to create the temporary tattoo. In other embodiments, an artificial tan can be created by delivering a colorant or, conversely, a tan can be prevented by delivering a sunscreen into the skin.

The increased permeability of the stratum corneum can be made painless or less painful for a subject by using lattices of thermal islets (or damage islets) rather than a continuous area of heating. Because the entire area and thickness of the skin is not

heated, a 40-43°C isotherm can be terminated near the epidermis/dermis boundary instead of deeper in the dermis. Therefore, nerve endings found in papillary dermis are not exposed to the 40-43°C temperatures associated with a pain response. As a result, the enhanced permeability paths defined by the thermal islets can be created without pain even though the SC has been exposed to temperatures significantly higher than 40-43°C.

A significant (orders of magnitude) increase in permeability of the stratum corneum occurs when the temperature of the extracellular lipids of the SC is raised to the transition temperature,  $T_m$ , at which the lipid state changes from the mesomorphic (liquid crystal) state to the liquid state ( $T_m=64^\circ\text{C}$  for rat SC, see Ogiso *et al.* (1996), *Biochim. Biophys. Acta* 1301(1-2):97-104). Simple estimates of the required heat flux to achieve this temperature, and thereby reversibly melt the lipid layers of the stratum corneum, can be made as follows.

For example, the thickness of the SC can be chosen to be  $d=15\text{ }\mu\text{m}$ , such as can be found on the volar forearm, for the purposes of this calculation. The stratum corneum (SC) is known to be composed of a mixture of water, lipids and proteins with the following approximate weights:  $W1=20\%$  water,  $W2=50\%$  lipids, and  $W3=30\%$  protein. The lipids of the SC are composed of the following: ceramides (50%), cholesterol (28%), free fatty acids (17%), and cholesterol sulfate (5%). The thermal parameters of the SC are determined to be the weighted sum of the corresponding parameters of the constituents with the appropriate weight factors  $W1$ ,  $W2$ , and  $W3$ :

| Constituent    | Weight factor | Density, g/cm <sup>3</sup> | Specific heat, J/(g K) | Thermal conductivity, W/(cm K) |
|----------------|---------------|----------------------------|------------------------|--------------------------------|
| Water          | 0.2           | 1                          | 4.18                   | 0.0058                         |
| Protein        | 0.3           | 1.3                        | 1.55                   | 0.00027                        |
| Lipids         | 0.5           | 0.31 (fat)                 | 0.975                  | 0.0022                         |
| Whole SC (Avg) | 1             | $\rho=0.745$               | $c=1.788$              | $\kappa=2.341\text{E-}3$       |

A typical initial SC temperature is  $T_0=30^\circ\text{C}$ . The latent heat of fusion,  $\lambda$ , (for melting) for the SC lipids is assumed to be similar in value to that known for the lipid DPPC (dipalmitoylphosphatidylcholine). This parameter is  $\lambda=14500\text{ J/mol}=2\text{ J/gm}$ , where the molecular weight is 734 gm/mole. Assuming the adiabatic mode (neglect heat



loss) and temperature equilibration among the constituents, the threshold fluence for melting the lipid,  $F_m$ , may be evaluated as follows:

$$F_m = [(T_m - T_0) \cdot c + \lambda] \cdot \rho \cdot d$$

Using the estimates of the parameters above, the value for the required fluence to melt the lipids of the SC is  $F_m = 0.07 \text{ J/cm}^2$ . This fluence may be achieved in a variety of ways as discussed herein. For example, EMR may be absorbed directly and converted to heat by one or more of the constituents acting as endogenous chromophores of the SC, or EMR may be absorbed by exogenous chromophores on the skin surface (*e.g.*, carbon dots). Note that the relative contribution of energy to actually melt the lipids is small ( $\sim 3\%$ ) and that most of the energy is needed to bring the SC from the ambient temperature,  $T_0$ , to the melting point,  $T_m$ .

$$\frac{\lambda}{[(T_m - T_0) \cdot c]} = 0.033$$

The thermal relaxation time,  $TRT$ , of the SC is estimated as follows:

$$\kappa := 2.341 \times 10^{-3} \cdot \frac{\text{watt}}{\text{cm} \cdot \text{K}} \quad \text{ms} := 10^{-3} \cdot \text{s}$$

$$TRT := \frac{d^2 \cdot \rho \cdot c}{2 \cdot \kappa} \quad TRT = 0.64 \text{ ms}$$

As an example, a heat flux of  $\sim 1 \text{ kWcm}^{-2}$  for  $70 \mu\text{s}$  will satisfy this condition. Note that if the melting point temperature needs to be maintained for a time exceeding the  $TRT$ , then the required heat flux must balance the heat loss once the required temperature is reached.

The size of the enhanced permeability paths can range from the diameter of an intercellular lipid space (*e.g.*,  $1 \mu\text{m}$ ) or the thickness of a horny cell (*e.g.*,  $0.5 \mu\text{m}$ ) at one extreme, to about the SC thickness (*e.g.*,  $10\text{-}500 \mu\text{m}$ ). Typically, however, the enhanced permeability paths are about  $20 \mu\text{m}$  to  $1 \text{ mm}$  in diameter and less than  $50 \mu\text{m}$  in depth to avoid damage to the viable epidermal layers, as well as to reduce or eliminate pain and discomfort. Nonetheless, for some embodiments, thermal islets can extend into deeper

layers of the epidermis and dermis to denature them and stimulate blood microcirculation for faster drug absorption in the body. Targeting deeper tissues with higher temperatures, however, could necessitate pain control for the patient.

Generally, the spacing of thermal islets should be as dense as possible to maximize the permeability and thus delivery efficiency. However, if the paths are too dense, then the depth-temperature selectivity is impacted. For example, if the spacing were zero, then heat would only effectively diffuse downward rather than radially, making it difficult to heat the stratum corneum sufficiently to produce enhanced permeability paths while preventing injury and pain to the deeper epidermal and dermal layers. Thus, generally, the fill factor is less than 30%, but greater than 1%, although it is not excluded that higher or lower percentage fill factors can be used for this application.

## 2. Thermal Islets in Deep Tissues

In accordance with the present invention, and as more fully described below, thermal islets can be produced which span from a tissue surface to deeper layers of the tissue, or which are present entirely in subsurface layers (see, *e.g.*, Fig. 2, islet 198). Such thermal islets can be used for applications such as thermally-enhanced photobiomodulation, photobiostimulation and photobiosuspension, as well as the creation of damage islets, as described below.

### C. Damage Islets

In some aspects, the invention provides methods of treating tissues by creating lattices of damage islets. These methods can be used in, for example, skin rejuvenation, tattoo removal (*e.g.*, killing cells containing ink particles, ablation of tattoo ink particles), acne treatment (*e.g.*, damaging or destroying sebaceous glands, killing bacteria, reducing inflammation), pigmented lesion treatment, vascular lesion treatment, and nevus flammeus ("port wine stain") removal (*e.g.*, reducing pathological vasculature), among others. Lattices of damage islets can also be used to increase the permeability of the stratum corneum. The time for recovery or healing of such damage islets can be controlled by changing the size of the damage islets and the fill factor of the lattice.

#### 1. Tissue Remodeling

In one embodiment, the invention provides methods of tissue remodeling based on controlled tissue damage.

One embodiment of tissue remodeling is skin "rejuvenation," a complex process involving one or more of (a) reduction in skin dyschromia (*i.e.*, pigment non-uniformities), (b) reduction in telangiectasia (*i.e.*, vascular malformations), (c) improvement in skin texture (*e.g.*, reduction of rhytides and wrinkles, skin smoothing, pore size reduction), and (d) improvement in skin tensile properties (*e.g.*, increase in elasticity, lifting, tightening). Techniques used for skin rejuvenation can be divided into three broad classes: ablative, non-ablative and fractional (including the lattices of islets of the present invention).

In the ablative resurfacing approach, the full thickness of the epidermis and a portion of upper dermis are ablated and/or coagulated. The ablative techniques typically deliver more pronounced clinical results, but entail considerable post-operative recovery time and care, discomfort, and risk of infection. For example, laser skin resurfacing (*e.g.*, using a CO<sub>2</sub> laser with an absorption coefficient of  $\sim 900\text{ cm}^{-1}$ , or an Er:YAG laser with an absorption coefficient of  $\sim 13,000\text{ cm}^{-1}$ ) requires weeks of recovery time, followed by a period of up to several months during which the treated skin is erythematous.

In the non-ablative approach, the zone of coagulation is shifted deeper into the tissue, with the epidermis being left intact (*e.g.*, using lasers with absorption coefficients of  $5\text{--}25\text{ cm}^{-1}$ ). The non-ablative techniques entail considerably less post-operative recovery time and care, discomfort, and risk of infection.

The fractional approach is also non-ablative but, instead of coagulating the entire treatment area or damage zone, entails partial or fractional damage of the treatment area. That is, a lattice of damage islets is created within the treatment area.

The present invention provides methods of skin rejuvenation in which thermal and damage islets can be relatively deep in the dermis and hypodermis (*e.g.*, depths  $> 500\text{ }\mu\text{m}$  from the skin surface). In order to prevent epidermal damage, active or passive cooling of the epidermis can be employed.

## 2. Lifting and Tightening Skin

The creation of lattices of damage islets can result in skin lifting or tightening as a result of (a) shrinkage of collagen fibrils subjected to elevated temperatures (immediate effect) or (b) coagulation of localized areas in the dermis and hypodermis (immediate to short-term effect).

### 3. Smoothing Skin Texture

The creation of lattices of damage islets can result in smoother skin texture as a result of coagulation of localized areas in the dermis and hypodermis (immediate to short-term effect). This technique also can be used for texturing tissues or organs other than the dermis/epidermis (*e.g.*, lip augmentation).

### 4. Promoting Collagen Production

The creation of lattices of damage islets can result in the promotion of collagen production as a result of the healing response of tissues to thermal stress or thermal shock (medium- to long-term effect).

### 5. Removing Tattoos

The creation of lattices of damage islets can be used to remove tattoos by killing the cells containing the tattoo ink particles (typically cells of the upper dermis). After these cells are killed, the tattoo ink is cleared away from the tissue site by normal scavenging processes. Alternatively, or in addition, lattices of damage islets can be used to remove tattoos by selecting the wavelength(s) of the EMR treatment to cause selective absorption of the EMR energy by the tattoo ink particles. In some embodiments, the pulse width of the incident pulse is chosen to match the thermal relaxation time of the ink particles. The absorption of the EMR energy by the tattoo ink particles can cause the cells to be heated and killed; can cause the ink particles to undergo photobleaching or be broken into smaller molecules which are removed by normal processes; or can otherwise cause the ink to be destroyed.

### 6. Increasing Permeability of the Stratum Corneum

The creation of lattices of damage islets can be used in order to increase the permeability of the stratum corneum by heating islets of tissue to temperatures higher than 100°C to create small holes in SC. Thus, in these embodiments, the EMR treatment coagulates, ablates, vaporizes, or otherwise damages or removes portions of the SC, including the crystalline intercellular lipid structure or cells, to form a lattice of damage islets through the SC. This method increases the permeability of the SC for a longer period of time than the thermal islet methods described above because the damaged areas or holes can remain in the SC until that layer of cells is replaced through the normal process of outgrowth from the stratum basale (*e.g.*, approximately 21-28 days).

### 7. Treating Acne

The creation of lattices of damage islets can be used to treat acne by selecting the wavelength(s) of the EMR treatment to cause selective absorption of the EMR energy by sebum, or targeting the lattice to sebaceous glands, in order to selectively damage or destroy the sebaceous glands. The EMR treatment can also be targeted to bacteria within acne sores.

### 8. Treating Hypertrophic Scars

The creation of lattices of damage islets can be used to treat hypertrophic scars by inducing shrinkage and tightening of the scar tissue, and replacement of abnormal connective tissue with normal connective tissue.

### 9. Reducing Body Odor

The creation of lattices of damage islets can be used to treat body odor by selectively targeting eccrine glands, thereby reducing the production of eccrine sweat or altering its composition.

### 10. Removing Warts and Calluses

The creation of lattices of damage islets can be used to treat warts and calluses by selectively targeting the pathological tissue to kill cells or cause tissue peeling. The pathological tissue can be replaced with normal tissue by normal biological processes.

### 11. Treating Psoriasis

The creation of lattices of damage islets can be used to treat psoriasis by using EMR of appropriate wavelength to selectively target psoriasis plaques, thereby stopping or reversing plaque formation. The pathological tissue can be replaced with normal tissue by normal biological processes.

### 12. Improving Wound and Burn Healing

The creation of lattices of damage islets can be used to decrease the time needed for the healing of wounds or burns (including frostbite) by increasing the wound or burn margin without substantially increasing the volume.

### 13. Reducing Cellulite or Fat volume

The creation of lattices of damage islets can be used to reduce cellulite by changing the mechanical stress distribution at the dermis/hypodermis border.

Alternatively, or in addition, lattices of damage islets can be used to reduce fat in the hypodermis (subcutaneous tissue) by heating and damaging fatty cells inside islets.

#### 14. Decreasing Body Hair

The creation of lattices of damage islets can be used in order to decrease the amount or presence of body hair by targeting lattices of damage islets to hair follicles in the skin. The methods can selectively target melanin or other chromophores present in hair or hair follicles, or may non-selectively target water in the hair follicle.

#### 15. Ablation or Welding of Internal Epithelia

The creation of lattices of damage islets can be used in order to damage or destroy internal epithelia to treat conditions such as a benign prostatic hyperplasia or hypertrophy, or restenosis. The methods can also be used to weld tissues together by creating damage areas at tissue interfaces.

#### 16. Creation of Identification Patterns

The creation of lattices of damage islets can be used in order to create identification patterns in tissues which result from the ablation of tissue or other structures, or which result from the tissue healing process. For example, patterns can be created in hair shafts by "etching" the hair with a lattice of damage islets. Alternatively, dermal, epidermal or other epithelial tissues can be patterned using the healing process to create defined areas with altered appearances.

#### D. Photochemical Islets

In some aspects, the invention provides methods of treating tissues by creating lattices of photochemical islets. These methods can be used in, for example, activating EMR-dependent biological responses (*e.g.*, melanin production or "tanning") and photodynamic therapy (*e.g.*, psoralen therapy for vitiligo or hypopigmentation). For example, vitiligo, white stretch marks (*i.e.*, striae alba), and hypo-pigmentation can be treated by creating photochemical islets which, with or without photodynamic agents, increase the production of pigmentation in the treated areas. In particular, by targeting the stratum basale, proliferation and differentiation of melanocytes can be promoted.

Products and Methods for Producing Lattices of EMR-Treated Islets

Figure 5 shows a broad overview schematic of an apparatus 100 that can be used in one embodiment of the invention to produce islets of treatment in the patient's skin. For this apparatus 230, optical energy 232 from a suitable energy source 234 passes through optical device 236, filter 238, cooling mechanisms 240, 242, and cooling or heating plate 244, before reaching tissue 246 (*i.e.*, the subject's skin). Each of these components is described in greater detail below. Generally, however, the EMR from the energy source 234 is focused by the optical device 236 and shaped by masks, optics, or other elements in order to create islets of treatment on the subject's skin. In some embodiments of the invention, certain of these components, such as, for example, filter 328 where a monochromatic energy source is utilized or optics 236, may not necessarily be present. In other embodiments, the apparatus may not contact the skin. In yet another embodiment, there is no cooling mechanism 4 such that there is only passive cooling between the contact plate and the skin.

A suitable optical impedance matching lotion or other suitable substance would typically be applied between plate 244 and tissue 246 to provide enhanced optical and thermal coupling. Tissue 246, as shown in Figure 5, is divided into an upper region 248, which, for applications where radiation is applied to the skin surface, would be the epidermis and dermis, and a lower region 250, which would be a subdermal region in the previous example. Region 250, for instance, can be the hypodermis.

Figure 6 shows a hand held device 260 which can contain the components of apparatus 230 set forth in connection with Figure 5. In particular, the housing 264 of hand held device 260 can contain the energy source 264, optical device 236, filter 238, and the cooling mechanism 240 and cooling plate 244 (only cooling plate 244 is shown in Figure 6). When in use, optical energy passes through the cooling plate 244 to contact the patient's skin. In some embodiments, the housing 264 can also support a button to activate the energy source.

The hand held device 260 of Figure 6 also includes a connection 266 for an umbilical cord or cable connection to a control or base unit (not shown) that can communicate through control signals with the hand held device 260. The control unit can include, for example, a supply of coolant for the cooling mechanism 244. In another

embodiment, the control unit can include power settings and the like for the energy source (not shown in Figure 6) within the hand held device 260. In addition, the control unit can include a microcomputer and controller to control certain features of the invention, as will be described below in greater detail. The cable connecting the control unit to the connection 266 of the hand held device 260 can include supply lines for coolant and wires for control and power of the hand held device 260. In another embodiment, the energy source may be contained in the base unit with the energy being delivered to the hand held device through the umbilical cord. For example, optical energy may be delivered through an optical fiber in the umbilical cord. In another embodiment, all components are contained in the hand held device such that there is no base unit.

Figs. 3A and 3B show another schematic representation of a system 208 for creating islets of treatment. Figures 3A and 3B show a system for delivering optical radiation to a treatment volume V located at a depth d in the patient's skin and having an area A. Figures 3A and 3B also show treatment or target portions 214 (*i.e.*, islets of treatment) in the patient's skin 200. A portion of a patient's skin 200 is shown, which portion includes an epidermis 202 overlying a dermis 204, the junction of the epidermis and dermis being referred to as the dermis-epidermis (DE) junction 206. The treatment volume may be at the surface of the patient's skin (*i.e.*,  $d = 0$ ) such that islets of treatment are formed in the stratum corneum. In addition, the treatment volume V may be below the skin surface in one or more skin layers or the treatment volume may extend from the skin surface through one or more skin layers.

The system 208 of Figures 3A and 3B can be incorporated within a hand held device, such as device 260 depicted in Figure 6. System 208 includes an energy source 210 to produce electromagnetic radiation (EMR). The output from energy source 210 is applied to an optical system 212, which is preferably in the form of a delivery head in contact with the surface of the patient's skin, as shown in Fig. 3B. The delivery head can include, for example, a contact plate or cooling element 216 that contacts the patient's skin, as is also shown in Figure 6 (with numeral 244). The system 208 can also include detectors 216 and controllers 218. The detectors 216 can, for instance, detect contact with the skin and/or the speed of movement of the device over the patient's skin and can,



for example, image the patient's skin. The controller 218 can be used, for example, to control the pulsing of an EMR source in relation to contact with the skin and/or the speed of movement of the hand piece.

Throughout this specification, the terms "head", "hand piece" and "hand held device" may be used interchangeably.

Each of these components is discussed in greater detail below.

#### A. Electromagnetic Radiation Sources

The energy source 210 may be any suitable optical energy source, including coherent and non-coherent sources, able to produce optical energy at a desired wavelength or a desired wavelength band or in multiple wavelength bands. The exact energy source 210, and the exact energy chosen, may be a function of the type of treatment to be performed, the tissue to be heated, the depth within the tissue at which treatment is desired, and of the absorption of that energy in the desired area to be treated. For example, energy source 210 may be a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, a fluorescent lamp, a light emitting diode, a laser (including diode and fiber lasers), the sun, or other suitable optical energy source. In addition, multiple energy sources may be used which are identical or different. For example, multiple laser sources may be used and they may generate optical energy having the same wavelength or different wavelengths. As another example, multiple lamp sources may be used and they may be filtered to provide the same or different wavelength band or bands. In addition, different types of sources may be included in the same device, for example, mixing both lasers and lamps.

Energy source 210 may produce electromagnetic radiation, such as near infrared or visible light radiation over a broad spectrum, over a limited spectrum, or at a single wavelength, such as would be produced by a light emitting diode or a laser. In certain cases, a narrow spectral source may be preferable, as the wavelength(s) produced by the energy source may be targeted towards a specific tissue type or may be adapted for reaching a selected depth. In other embodiments, a wide spectral source may be preferable, for example, in systems where the wavelength(s) to be applied to the tissue may change, for example, by applying different filters, depending on the application. Acoustic, RF or other EMF sources may also be employed in suitable applications.

For example, UV, violet, blue, green, yellow light or infrared radiation (*e.g.*, about 290-600 nm, 1 400 – 3000 nm) can be used for treatment of superficial targets, such as vascular and pigment lesions, fine wrinkles, skin texture and pores. Blue, green, yellow, red and near IR light in a range of about 450 to about 1300 nm can be used for treatment of a target at depths up to about 1 millimeter below the skin. Near infrared light in a range of about 800 to about 1400 nm, about 1500 to about 1800 nm or in a range of about 2050 nm to about 2350 nm can be used for treatment of deeper targets (*e.g.*, up to about 3 millimeters beneath the skin surface) -- (See Table 1B).

### 1. Coherent Light Sources.

The energy source 210 can be any variety of a coherent light source, such as a solid-state laser, dye laser, diode laser, fiber laser, or other coherent light source. For example, the energy source 210 can be a neodymium (Nd) laser, such as a Nd:YAG laser. In this exemplary embodiment, the energy source 210 includes a neodymium (Nd) laser generating radiation having a wavelength around 1064 nm. Such a laser includes a lasing medium, *e.g.*, in this embodiment a neodymium YAG laser rod (a YAG host crystal doped with Nd<sup>+3</sup> ions), and associated optics (*e.g.*, mirrors) that are coupled to the laser rod to form an optical cavity for generating lasing radiation. In other embodiments, other laser sources, such as chromium (Cr), Ytterbium (Yt) or diode lasers, or broadband sources, *e.g.*, lamps, can be employed for generating the treatment radiation.

Lasers and other coherent light sources can be used to cover wavelengths within the 100 to 100,000 nm range. Examples of coherent energy sources are solid state, dye, fiber, and other types of lasers. For example, a solid state laser with lamp or diode pumping can be used. The wavelength generated by such a laser can be in the range of 400 – 3,500 nm. This range can be extended to 100 – 20,000 nm by using non-linear frequency converting. Solid state lasers can provide maximum flexibility with pulse width range from femtoseconds to a continuous wave.

Another example of a coherent source is a dye laser with non-coherent or coherent pumping, which provide wavelength-tunable light emission. Dye lasers can utilize a dye dissolved either in liquid or solid matrices. Typical tunable wavelength bands cover 400 – 1,200 nm and a laser bandwidth of about 0.1 – 10 nm. Mixtures of different dyes can provide multi wavelength emission. Dye laser conversion efficiency is

about 0.1 – 1 % for non-coherent pumping and up to about 80 % with coherent pumping. Laser emission could be delivered to the treatment site by an optical waveguide, or, in other embodiments, a plurality of waveguides or laser media could be pumped by a plurality of laser sources (lamps) next to the treatment site. Such dye lasers can result in energy exposure up to several hundreds of  $J/cm^2$ , pulse duration from picoseconds to tens of seconds, and a fill factor from about 0.1% to 90 %.

Another example of a coherent source is a fiber laser. Fiber lasers are active waveguides a doped core or undoped core (Raman laser), with coherent or non-coherent pumping. Rare earth metal ions can be used as the doping material. The core and cladding materials can be quartz, glass or ceramic. The core diameter could be from microns to hundreds of microns. Pumping light could be launched into the core through the core facet or through cladding. The light conversion efficiency of such a fiber laser could be up to about 80% and the wavelength range can be from about 1,100 to 3,000 nm. A combination of different rare-earth ions, with or without additional Raman conversion, can provide simultaneous generation of different wavelengths, which could benefit treatment results. The range can be extended with the help of second harmonic generation (SHG) or optical parametric oscillator (OPO) optically connected to the fiber laser output. Fiber lasers can be combined into the bundle or can be used as a single fiber laser. The optical output can be directed to the target with the help of a variety of optical elements described below, or can be directly placed in contact with the skin with or without a protective/cooling interface window. Such fiber lasers can result in energy exposures of up to about several hundreds of  $J/cm^2$  and pulse durations from about picoseconds to tens of seconds.

Diode lasers can be used for the 400 –100,000 nm range. Since many photodermatology applications require a high-power light source, the configurations described below using diode laser bars can be based upon about 10 –100 W, 1-cm-long, cw diode laser bar. Note that other sources (*e.g.*, LEDs and microlasers) can be substituted in the configurations described for use with diode laser bars with suitable modifications to the optical and mechanical sub-systems.

Other types of lasers (*e.g.*, gas, excimer, etc.) can also be used.

## 2. Non-Coherent Light Sources

A variety of non-coherent sources of electromagnetic radiation (*e.g.*, arc lamps, incandescence lamps, halogen lamps, light bulbs) can be used in the invention for the energy source 210. There are several monochromatic lamps available such as, for example, hollow cathode lamps (HCL) and electrodeless discharge lamps (EDL). HCL and EDL could generate emission lines from chemical elements. For example, sodium emits bright yellow light at 550 nm. The output emission could be concentrated on the target with reflectors and concentrators. Energy exposures up to about several tens of J/cm<sup>2</sup>, pulse durations from about picoseconds to tens of seconds, and fill factors of about 1% to 90 % can be achieved.

Linear arc lamps use a plasma of noble gases overheated by pulsed electrical discharge as a light source. Commonly used gases are xenon, krypton and their mixtures, in different proportions. The filling pressure can be from about several torr to thousands of torr. The lamp envelope for the linear flash lamp can be made from fused silica, doped silica or glass, or sapphire. The emission bandwidth is about 180-2,500 nm for clear envelope, and could be modified with a proper choice of dopant ions inside the lamp envelope, dielectric coatings on the lamp envelope, absorptive filters, fluorescent converters, or a suitable combination of these approaches.

In some embodiments, a Xenon-filled linear flash lamp with a trapezoidal concentrator made from BK7 glass can be used. As set forth in some embodiments below, the distal end of the optical train can, for example, be an array of microprisms attached to the output face of the concentrator. The spectral range of EMR generated by such a lamp can be about 300 – 2000 nm, energy exposure can be up to about 1,000 J/cm<sup>2</sup>, and the pulse duration can be from about 0.1ms to 10s.

Incandescent lamps are one of the most common light sources and have an emission band from 300 to 4,000 nm at a filament temperature of about 2,500 C. The output emission can be concentrated on the target with reflectors and/or concentrators. Incandescent lamps can achieve energy exposures of up to about several hundreds of J/cm<sup>2</sup> and pulse durations from about seconds to tens of seconds.

Halogen tungsten lamps utilize the halogen cycle to extend the lifetime of the lamp and permit it to operate at an elevated filament temperature (up to about 3,500 C),

which greatly improves optical output. The emission band of such a lamp is in the range of about 300 to 3,000 nm. The output emission can be concentrated on the target with reflectors and/or concentrators. Such lamps can achieve energy exposures of up to thousand of J/cm<sup>2</sup> and pulse durations from about 0.2 seconds to continuous emission.

Light-emitting diodes (LEDs) that emit light in the 290-2,000 nm range can be used to cover wavelengths not directly accessible by diode lasers.

Referring again to Figures 3A and 3B, the energy source 210 or the optical system 212 can include any suitable filter able to select, or at least partially select, certain wavelengths or wavelength bands from energy source 210. In certain types of filters, the filter may block a specific set of wavelengths. It is also possible that undesired wavelengths in the energy from energy source 210 may be wavelength shifted in ways known in the art so as to enhance the energy available in the desired wavelength bands. Thus, filter may include elements designed to absorb, reflect or alter certain wavelengths of electromagnetic radiation. For example, filter may be used to remove certain types of wavelengths that are absorbed by surrounding tissues. For instance, dermis, hypodermis and epidermis tissues are primarily composed of water, as is much of the rest of the human body. By using a filter that selectively removes wavelengths that excite water molecules, the absorption of these wavelengths by the body may be greatly reduced, which may contribute to a reduction in the amount of heat generated by light absorption in these molecules. Thus, by passing radiation through a water-based filter, those frequencies of radiation that may excite water molecules will be absorbed in the water filter, and will not be transmitted into tissue. Thus, a water-based filter may be used to decrease the amount of radiation absorbed in tissue above the treatment region and converted into heat. For other treatments, absorption of the radiation by water may be desired or required for treatment.

### B. Optical System

Generally, optical system 212 of Figures 3A and 3B functions to receive radiation from the source 210 and to focus/concentrate such radiation to one or more beams 222 directed to a selected one or more treatment or target portions 214 of volume V, the focus being both to the depth d and spatially in the area A (see Figure 3B). Some embodiments of the invention use such an optical system 212, and other embodiments do not use an

optical system 212. In some embodiments, the optical system 212 creates one or more beams which are not focused or divergent. In embodiments with multiple sources, optical system 212 may focus / concentrate the energy from each source into one or more beams and each such beam may include only the energy from one source or a combination of energy from multiple sources.

If an optical system 212 is used, the energy of the applied light can be concentrated to deliver more energy to target portions 214. Depending on system parameters, portions 214 may have various shapes and depths as described above.

The optical system 212 as shown in Figs. 3A and 3B may focus energy on portions 214 or a selected subset of portions 214 simultaneously. Alternatively, the optical system 212 may contain an optical or mechanical-optical scanner for moving radiation focused to depth *d* to successive portions 214. In another alternative embodiment, the optical system 212 may generate an output focused to depth *d* and may be physically moved on the skin surface over volume *V*, either manually or by a suitable two-dimensional or three-dimensional (including depth) positioning mechanism, to direct radiation to desired successive portions 214. For the two later embodiments, the movement may be directly from portion to portion to be focused on or the movement may be in a standard predetermined pattern, for example a grid, spiral or other pattern, with the EMR source being fired only when over a desired portion 214.

Where an acoustic, RF or other non-optical EMR source is used as energy source 210, the optical system 212 can be a suitable system for concentrating or focusing such EMR, for example a phased array, and the term "optical system" should be interpreted, where appropriate, to include such a system.

### C. Cooling Elements.

As set forth above, the system 208 can also include a cooling element 215 to cool the surface of the skin 200 over treatment volume *V*. As shown in Figs. 3A and 3B, a cooling element 215 can act on the optical system 212 to cool the portion of this system in contact with the patient's skin, and thus the portion of the patient's skin in contact with such element. In some embodiments of the invention intended for use on the stratum corneum, the cooling element 215 might not be used or, alternatively, might not be cooled during treatment (*e.g.*, cooling only applied before and/or after treatment). In

some embodiments, cooling can be applied fractionally on a portion of the skin surface (cooling islets), for example, between optical islets. In some embodiments, cooling of the skin is not required and a cooling element might not be present on the hand piece. In other embodiments, cooling may be applied only to the portions of tissue between the treatment islets in order to increase contrast.

The cooling element 215 can include a system for cooling the optical system (and hence the portion in contact with the skin) as well as a contact plate that touches the patient's skin when in use. The contact plate can be, for example, a flat plate, a series of conducting pipes, a sheathing blanket, or a series of channels for the passage of air, water, oil or other fluids or gases. Mixtures of these substances may also be used, such as a mixture of water and methanol. For example, in one embodiment, the cooling system can be a water-cooled contact plate. Figure 6, for example, shows a cooling plate 244 that is in contact with the person's skin when in use. In another embodiment, the cooling mechanism may be a series of channels carrying a coolant fluid or a refrigerant fluid (for example, a cryogen), which channels are in contact with the patient's skin 200 or with a plate of the apparatus 208 that is in contact with the patient's skin. In yet another embodiment, the cooling system may comprise a water or refrigerant fluid (for example R134A) spray, a cool air spray or air flow across the surface of the patient's skin 200. In other embodiments, cooling may be accomplished through chemical reactions (for example, endothermic reactions), or through electronic cooling, such as Peltier cooling. In yet other embodiments, cooling mechanism 215 may have more than one type of coolant, or cooling mechanism 215 and/or contact plate may be absent, for example, in embodiments where the tissue is cooled passively or directly, for example, through a cryogenic or other suitable spray. Sensors or other monitoring devices may also be embedded in cooling mechanism 215 or other portions of the hand held device, for example, to monitor the temperature, or determine the degree of cooling required by the patient's skin 200, and may be manually or electronically controlled.

In certain cases, cooling mechanism 215 may be used to maintain the surface temperature of the patient's skin 200 at its normal temperature, which may be, for example, 37 or 32 °C, depending on the type of tissue being heated. In other embodiments, cooling mechanism 215 may be used to decrease the temperature of the

surface of the patient's skin 200 to a temperature below the normal temperature of that type of tissue. For example, cooling mechanism 215 may be able to decrease the surface temperature of tissue to, for example, a range between 25 °C and -5 °C. In other embodiments, a plate can function as a heating plate in order to heat the patient's skin. Some embodiments can include a plate that can be used for cooling and heating.

A contact plate of the cooling element 215 may be made out of a suitable heat transfer material, and also, where the plate contacts the patient's skin 200, of a material having a good optical match with the tissue. Sapphire is an example of a suitable material for the contact plate. Where the contact plate has a high degree of thermal conductivity, it may allow cooling of the surface of the tissue by cooling mechanism 215. In other embodiments, contact plate may be an integral part of cooling mechanism 215, or may be absent. In some embodiments of the invention, such as shown in Figs. 3A and 3B, energy from energy source 210 may pass through contact plate. In these configurations, contact plate may be constructed out of materials able to transmit at least a portion of energy, for example, glass, sapphire, or a clear plastic. In addition, the contact plate may be constructed in such a way as to allow only a portion of energy to pass through contact plate, for example, via a series of holes, passages, apertures in a mask, lenses, etc. within the contact plate. In other embodiments of the invention, energy may not be directed through the cooling mechanism 215.

In certain embodiments of the invention, various components of system 208 may require cooling. For example, in the embodiment shown in Figs. 3A and 3B, energy source 210, optics 212, and filter may be cooled by a cooling mechanism (not shown). The design of cooling mechanism may be a function of the components used in the construction of the apparatus. The cooling element 215 for the patient's skin 200 and the cooling element for the components of the system 208 may be part of the same system, separate systems or one or both may be absent. Cooling mechanism for the components of the system 208 may be any suitable cooling mechanism known in the art. Cooling of the components may be accomplished through convective or conductive cooling. In some embodiments, the cooling element can prevent optics 212 from overheating due absorption of EMR.



#### D. Devices for Producing a Multiplicity of Treated Islets

A number of different devices and structures can be used to spatially modulate and/or concentrate EMR in order to generate islets of treatment in the skin. For example, the devices can use reflection, refraction, interference, diffraction, and deflection of incident light to create treatment islets. A number of these devices are briefly summarized below, with a more detailed explanation of the devices in the remainder of the specification, and in particular in connection with the section entitled Devices and Systems for Producing Islets of Treatment, Example 4. Methods for generating islets of treatment, and numerous other devices and methods for creating islets of treatment are set forth throughout this specification. In addition, although some devices and methods for generating islets of treatment are briefly set forth below, the invention is not limited to these particular methods and devices.

Splitting of EMR by reflection of the light can be obtained using specular or diffuse reflection of the light from surfaces with refractive indices higher than 1. Splitting of EMR by refraction can be obtained using refraction on angular or curved surfaces. Diffraction splitting is based on the fact that light can bend around edges. Deflection splitting can be achieved when light propagates inside a media with a non-even distribution of refractive indices.

##### 1. Blocking Portions of the EMR Beam

In some embodiments, a mask can be used to block portions of the EMR generated by the EMR source from reaching the tissue. The mask can contain a number of holes, lines, or slits, which function to spatially modulate the EMR to create islets of treatment. Figures 7 and 8 illustrate two embodiments of the invention in which the islets of treatment are formed generally through the use of a mirror containing holes or other transmissive portions. Light passes through the holes in the mirror and strikes the patient's skin, creating islets of treatment. Light reflected by the mirror stays in the optical system through a system of reflectors and may be redirected through the holes to improve efficiency. One effective mask is a contact cooling mask (*i.e.*, it contacts the skin during treatment) with a high reflection and minimum absorption for masking light.

##### 2. Focusing, Directing, or Concentrating the EMR Beam

In some embodiments, spatial modulation and concentration of the EMR can be achieved by shaping an end portion of a light guide with prisms, pyramids, cones, grooves, hemispheres, or the like in order to create output light spatial modulation and concentration, and therefore to form islets of treatment in a patient's skin. For example, Figures 9A through 10A depict such embodiments. Numerous exemplary types of imaging optics and/or diffractive optics that can also be used in this embodiment of the invention are set forth in the section entitled Devices and Systems for Creation of Islets (Example 2) below.

In addition, in some embodiments, such as that of Figure 10A-10C, the end of the light guide can be shaped in order to introduce light total internal reflection (TIR) when the distal end of the device is in contact with air, while allowing EMR to pass through when the distal end is in contact with a lotion or skin surface.

Alternatively, some embodiments can use spatially modulated phase arrays to introduce phase shifts between different portions of the incident beam. As a result of interference between the said portions, amplitude modulation is introduced in the output beam.

### 3. Arrays of EMR Sources

Instead of splitting the EMR into multiple beams, one can use a plurality of light sources or a single light source with a serial or parallel optical multiplexer to form islets of treatment in the patient's skin. For example, the embodiment of Figure 11 uses a line or array of non-coherent EMR sources to create islets of treatment. Other embodiments of the invention, such as that shown in Figure 12C, use an array of diode laser bars in order to form islets of treatment. Still other embodiments use a bundle of optical fibers to deliver spatially modulated EMR to the patient's skin. Figures 12E, 13B-D, and 14A are exemplary embodiments that use a bundle of optical fibers.

### 4. Pulsing the EMR Source

In some embodiments, the invention can include a sensor for determining the speed of movement of the hand piece across the target area of the patient's skin. The hand piece can further include circuitry in communication with the sensor for controlling the optical energy in order to create islets of treatment. The circuitry can control, for example, pulsing of the optical energy source based on the speed of movement of the

head portion across the skin in order to create islets of treatment. In another embodiment, the circuitry can control movement of the energy source, a scanner or other mechanism within the apparatus based on the speed of movement of the head portion across the skin in order to expose only certain areas of the skin to the EMR energy as the head is moved over the skin in order to create islets of treatment. Figures 15 and 16 are exemplary embodiments according to this aspect of the invention.

#### 5. Lattices of Exogenous Chromophores

In other embodiments, spatially selective islets of treatment can be created by applying to the skin surface a desired pattern of a topical composition containing a preferentially absorbing exogenous chromophore. The chromophore can also be introduced into the tissue with a needle, for example, a micro needle as used for tattoos. In this case, the EMR energy may illuminate the entire skin surface where such pattern of topical composition has been applied. Upon application of appropriate EMR, the chromophores can heat up, thus creating islets of treatment in the skin. Alternatively, the EMR energy may be focused on the pattern of topical composition. A variety of substances can be used as chromophores in the invention including, but not limited to, carbon, metals (Au, Ag, Fe, etc.), organic dyes (Methylene Blue, Toluidine Blue, etc.), non-organic pigments, nanoparticles (such as fullerenes), nanoparticles with a shell, carbon fibers, etc. The desired pattern can be random and need not be regular or predetermined. It can vary as a function of the skin condition at the desired treatment area and be generated *ad hoc*.

In some embodiments, the invention provides a film or substrate material with a lattice of dots, lines or other shapes, either on the surface of the film or embedded within the film, in which the dots, lines or other shapes include a chromophore appropriate to the EMR source. The dots, lines or other shapes may be the same or different sizes and different shapes may be included on the film.

The dots, lines or other shapes may be formed from a material that can be glued, welded or otherwise attached to the stratum corneum to create islets, and such attachment may be sufficient to allow the film to be removed from the skin while leaving the dots, lines or other shapes on the skin. For example, the dots, lines or other shapes may be formed of an ultraviolet curing compound such that when the film is applied to the skin

and ultraviolet light is applied to the film, the dots, lines or other shapes are attached to the skin and the film may be removed prior to EMR energy being applied. In other cases, the dots, lines or other shapes may be formed of a suitable phase-changing material (*e.g.*, albumin), which can be used for welding. In other cases, the film is not removed and the EMR energy is applied through the film.

In other methods, the dots, lines or other shapes may be manually applied to the skin individually or by spraying or other techniques. In other embodiments, the hand piece may apply the shapes to the skin prior to applying the EMR energy. As one example, the shapes may be contained in a lotion, gel, powder or other topical composition that is applied to the skin manually prior to using the hand piece to apply the EMR energy. Alternatively, the lotion is dispensed by the hand piece onto the skin prior to the hand piece delivering EMR energy. As another example, a film containing the shapes may be applied to the skin manually or by the hand held device (as for example a tape dispenser).

#### 6. Creating thermal lattices using patterned cooling

Some embodiments can produce thermal (and damage) lattices (or treatment islets) by employing uniform EMR beams and spatially modulated cooling devices. The resulting thermal lattice in such cases will be inverted with respect to the original cooling matrix.

#### E. Controllers and Feedback Systems

Some embodiments of the invention can also include speed sensors, contact sensors, imaging arrays, and controllers to aid in various functions of applying EMR to the patient's skin. System 208 of Fig. 3A includes an optional detector 216, which may be, for example, a capacitive imaging array, a CCD camera, a photodetector, or other suitable detector for a selected characteristic of the patient's skin. The output from detector 216 can be applied to a controller 218, which is typically a suitably programmed microprocessor or other such circuitry, but may be special purpose hardware or a hybrid of hardware and software. Control 218 can, for example, control the turning on and turning off of the light source 210 or other mechanism for exposing the light to the skin (*e.g.*, shutter), and control 218 may also control the power profile of the radiation. Controller 218 can also be used, for example, to control the focus depth for the optical

system 212 and to control the portion or portions 214 to which radiation is focused/concentrated at any given time. Finally, controller 218 can be used to control the cooling element 215 to control both the skin temperature above the volume V and the cooling duration, both for pre-cooling and during irradiation.

#### F. Creation of Lattices Using Non-optical EMR Sources

The lattices of the invention can also be produced using non-optical sources. For example, as noted above, microwave, radio frequency and low frequency or DC EMR sources can be used as energy sources to create lattices of EMR-treated islets. In addition, for treating tissue surfaces, the tissue surface can be directly contacted with heating elements in the pattern of the desired lattice.

The following examples illustrate some preferred modes of practicing the present invention, but are not intended to limit the scope of the claimed invention. Alternative materials and methods may be utilized to obtain similar results.

### EXAMPLE 1

#### Computational and Theoretical Models of Islets and Islet Formation

The optical, thermal and damage islets models described above were analyzed using computational models. To get a three-dimensional optical islet below the skin surface and limited from all sides, the beam can be focused into the skin. Three dimensional thermal or damage islets below the skin surface can be produced using three dimensional optical islets or using skin surface cooling in combination with optical beams with converted, diverged or collimated beams. On the other hand, two-dimensional and one-dimensional islets below or including the skin surface and three-dimensional islets including the skin surface can be obtained using a collimated beam incident normal to the skin surface. For this reason, the effects of both collimated and focused beams were considered. Furthermore, the procedures emphasized here are those where the thermal and damage islets appear due to the light absorption by the tissue water rather than by other chromophores (*i.e.*, melanin and hemoglobin). This mechanism is characteristic for treatment in the near infrared (NIR) range. As a standard example, type II skin per Fitzpatrick's classification (Fitzpatrick (1998), *Arch. Dermatol.* 124:869-71)

was used and the wavelength of light was assumed to be 800 nm or longer. The light pulses were generally assumed to be rectangular.

To handle the periodicity of the islets, periodic boundary conditions for light and temperature were applied at the relevant interfaces between the voxels (*i.e.*, the periodically repeated cells that comprise the lattice, where each cell includes an islet and a portion of the space surrounding the islet). More precisely, the voxel interfaces were considered as the heat insulating surfaces showing perfect light reflection. This technique allows evaluation of solutions for light transport and heat equations within one voxel only, which can then be propagated periodically to the whole lattice.

#### A. Computational model of skin.

Skin was approximated by a planar four-layer structure exhibiting cylindrical symmetry as shown in Fig. 63. The particular layers included into the model were the upper layer incorporating the stratum corneum and the 3 upper layers of epidermis: the basal layer of epidermis, the reticular dermis with the upper vessel plexus, and the dermis.

In the visible and NIR spectral ranges, the absorption coefficient of each layer includes contributions from the three basic chromophores: blood, melanin, and water. The corresponding expression can be written as:

$$\mu_{a_k} = B_k C_k(\lambda) \mu_{ab}(\lambda) + (1 - B_k - W_k) \cdot \mu_{aT}(\lambda) + M_k \mu_{aM}(\lambda) + W_k \mu_{aW}(\lambda), \quad (A1)$$

where  $k = 1 \dots 4$  is the layer number,  $M_k$ ,  $B_k$  and  $W_k$  are the volume fractions of melanin, blood and water in the layer (factor  $M_k$  is unity for the melanin containing layers including the upper and basal layers and  $M_k$  is zero for the other layers),  $C_k$  is the correction factor,  $\mu_{ab}(\lambda)$ ,  $\mu_{aM}(\lambda)$ ,  $\mu_{aW}(\lambda)$  and  $\mu_{aT}(\lambda)$  are the absorption coefficients of blood, melanin, water, and the background tissue absorption, respectively. The latter absorption coefficient is suggested to be wavelength independent and equal to  $0.015 \text{ mm}^{-1}$ . This value was obtained from the comparison of the measured and

calculated spectra of the skin reflection near 800 nm, where the absorption of the main three chromophores is very small.

The correction factors are the numbers from zero through unity taking into account the fact that blood is confined to the vessels rather than being distributed homogeneously in the tissue bulk. If the vessel is thick enough, the light cannot penetrate to its inner part and, therefore, the interior of the vessel does not work as an absorber. If this is the case the correction factor is appreciably smaller than unity. Conversely, for very thin vessels the correction factor is close to unity. It follows that the correction factor depends on the mean vessel diameter and the blood absorption coefficient at the particular wavelength. To evaluate these factors, numeric data from (Verkruijsse *et al.* (1997), *Physics in Medicine and Biology* 42: 51-65) were used.

Several publications address the absorption spectrum of blood (see, *e.g.*, Roggan *et al.* (1999), *Biomedical Optics* 4: 36-46; Yaroslavsky *et al.* (1996), *Proc. SPIE* 2678: 314-24; Svaasand *et al.* (1995), *Lasers in Medical Science* 10: 55-65). The generally accepted relation is:

$$\mu_{ab}(\lambda) = (1-H) \cdot \mu_a W(\lambda) + H \cdot (OS \cdot \mu_{aHbO_2}(\lambda) + (1-OS) \cdot \mu_{aHb}(\lambda)) , \quad (A2)$$

where H is the hematocrit (*i.e.* the percentage of blood volume occupied by red blood cells), OS is the oxygen saturation,  $\mu_{aHb}(\lambda)$  and  $\mu_{aHbO_2}(\lambda)$  are the wavelength dependent absorption coefficients of hemoglobin and oxyhemoglobin, respectively. In this invention, typical values of 0.4 for the hematocrit and 0.8 for the OS were used, the latter being the average value for the venous (0.7) and arterial (0.9) blood. The absorption spectra of hemoglobin and oxyhemoglobin, in turn, may be approximated by sums of the Gaussian bands. The intensities and widths of the bands can be found in (Douven *et al.* (2000), *Proc SPIE* 3914: 312-23).

Being the turbid medium, blood affects the scattering coefficient of the layer where it is present. The effect of blood on the total scattering coefficient is introduced by the relation (Douven *et al.* (2000), *Proc SPIE* 3914: 312-23):

$$\mu s_k(\lambda) = B_k C_k \mu s_b(\lambda) + (1 - B_k) \cdot \mu s T_k(\lambda), \quad (A3)$$

where the total scattering coefficient of blood is given by

$$\mu s_b(\lambda) = \mu s_0 \cdot H \cdot (1 - H) \cdot (1.4 - H) \cdot \left( \frac{685 \text{ nm}}{\lambda} \right), \quad \mu s_0 = 440.72 \cdot \text{mm}^{-1}, \quad (A4)$$

and the anisotropy factor of the blood scattering is assumed constant over the visible and NIR wavelength ranges:

$$g_b = 0.995. \quad (A5)$$

The total scattering coefficient of the bloodless tissue,  $\mu s T_k$ , falls with the increase of wavelength. There are several empirical relations reported in the literature to describe this dependence (Douven *et al.* (2000), *Proc SPIE* 3914: 312-23; Jacques (1996) In *Advances in Optical Imaging and Photon Migration* eds. Alfano *et al.* 2: 364-71). These relations break down above 1000 nm where the decrease of the scattering coefficient becomes very slow (Troy *et al.* (2001), *Journal of Biomedical Optics* 6: 167-176). To cover both the visible and NIR ranges, the expression for the total scattering coefficient of the bloodless tissue was rearranged in the following way:

$$\mu s T_k(\lambda) = \begin{cases} \mu s_0_k \cdot \left( \frac{577 \text{ nm}}{\lambda} \right), & \lambda < 950 \text{ nm}, \\ \text{const}(\lambda), & \lambda \geq 950 \text{ nm}, \end{cases} \quad (A6)$$

where  $\mu s_0_k$  are the scattering coefficients at the reference wavelength 577 nm listed in Table 1.



The expression for the anisotropy of scattering was constructed to include the contribution from blood in the same manner as expression (A3):

$$g_k(\lambda) = \frac{B_k C_k \mu_s b(\lambda) g_b + (1 - B_k) \cdot \mu_s T_k(\lambda) \cdot gT(\lambda)}{\mu_s k}, \quad (A7)$$

where  $gT(\lambda)$  is the anisotropy factor of the bloodless tissue. The latter factor is an increasing function of wavelength below 1000 nm and measurements using the integrated sphere technique suggest that  $gT(\lambda)$  does not exceed 0.9 for  $1000 \text{ nm} < \lambda < 1900 \text{ nm}$  (Troy *et al.* (2001), *Journal of Biomedical Optics* 6: 167-176). Therefore, to describe the wavelength dependence of the anisotropy factor of the bloodless tissue, the corresponding expression from (Tsai *et al.* (1999), *Proc. SPIE* 3601: 327-334) from above was limited at  $gT(\lambda) = 0.9$  yielding:

$$gT(\lambda) = \begin{cases} 0.7645 + 0.2355 \cdot \left[ 1 - \exp\left(-\frac{\lambda - 500 \text{ nm}}{729.1 \text{ nm}}\right) \right], & \lambda < 1125 \text{ nm}, \\ 0.9, & \lambda \geq 1125 \text{ nm}. \end{cases} \quad (A8)$$

Melanin is confined entirely to the epidermis with its total concentration depending on the skin type. In the context of the four-layer model used in this invention, there are two layers containing melanin: the upper and basal layers. The partitioning of melanin between the two layers depends on the skin type as well. For light skin melanin is confined mainly to the basal layer, while for dark skin the distribution of melanin in the epidermis is somewhat more homogeneous. The fraction of melanin in the basal layer was assumed to be 50% for skin types V and VI and 70% for the other skin types (Fitzpatrick (1998), *Arch. Dermatol.* 124: 869-71). The total amount of melanin is characterized by the optical density (OD) of the epidermis, that is, the product of the melanin absorption coefficient and the epidermal thickness. In the model described by this invention, the total OD is the sum of contributions from the upper and basal layers.

Despite the OD variability due to many factors, for instance, tanning, the typical OD values listed in Table 1 were used here. These values are pertinent to the reference wavelength  $\lambda_{th} \approx 800 \text{ nm}$ .

Melanin OD in the infrared range can be described by the following relation:

$$OD(\lambda) = \begin{cases} OD(800 \text{ nm}) \cdot \exp\left(-\frac{\lambda - 800 \text{ nm}}{182 \text{ nm}}\right), & \lambda \leq \lambda_r = 1000 \text{ nm}, \\ OD(1000 \text{ nm}) \cdot \left(\frac{\lambda}{1000 \text{ nm}}\right)^{-2.14}, & \lambda > \lambda_r. \end{cases} \quad (\text{A9})$$

The absorption spectrum of water in the visible and near-IR may be found in the literature (Hale *et al.* (1973), *Applied Optics* 12: 555-63; Querry *et al.* (1978), *Applied Optics* 17: 3587-92). The volume fractions of water in the skin layers are listed in Table 1. The indices of refraction of the layers were assumed to be constant through the visible and NIR ranges and are listed in Table 1.

Thermal parameters of the skin layers were evaluated by applying Takata's relations (Takata *et al.* (1977) Laser induced thermal damage in skin. Report SAM-TR-77-38 Brooks Air Force Base (TX: US Air Force School for Aero-space Medicine)) yielding the density, the specific heat, and the thermal conductivity of a soft tissue as a function of the water content. The values obtained in this way are listed in Table 1 together with the thermal parameters of the sapphire window.

Degrees of damage were quantified by comparing the fractions of the undamaged and coagulated tissues at a particular site. Let  $c(t)$  be the fraction of the undamaged tissue at time  $t$ , so that  $c(0) = 1$ . The fraction of the coagulated tissue is given by  $1 - c(t)$ .

The kinetic model of the tissue damage yields relation  $\frac{d}{dt}\Omega(t) = F(T(t))$ ,

where  $\Omega(t) \equiv \ln(c(0)/c(t))$ , and  $F(T)$  is a function of the absolute temperature (in Kelvin) called the damage function (Pearce *et al.* (1995), In Optical-thermal response of laser-irradiated tissue eds. Welch *et al.* (NY and London: Plenum Press) pp. 561-606). The damage function used in this invention was (Pearce *et al.* (1995) In Optical-thermal

response of laser-irradiated tissue eds. Welch *et al.* (NY and London: Plenum Press) pp. 561-606; Henriques (1947), *Arch. Pathol.* 43: 480-502; Henriques *et al.* (1947), *Am. J. Pathol.* 23: 531-49; Moritz *et al.* (1947), *Am. J. Pathol.* 23:695-720; Wright (2003), *J. Biomech. Eng.* 125: 300-04):

$$F(T) = A \cdot \exp\left(-\frac{E_a}{R \cdot T}\right), \quad (\text{A10})$$

where  $R=8.31$  J/(mole·K) is the universal gas constant,  $A$  is the rate constant, and  $E_a$  is the activation energy of the coagulation process. Given the damage function (A10), the Arrhenius damage integral was obtained:

$$\Omega(t) = A \cdot \int_0^t \exp\left(-\frac{E_a}{R \cdot T(t')}\right) dt', \quad (\text{A11})$$

which is a measure of the damage degree (Pearce *et al.* (1995) In Optical-thermal response of laser-irradiated tissue eds. Welch *et al.* (NY and London: Plenum Press) pp. 561-606). The apparent inconvenience in using this measure is that the Arrhenius integral tends to infinity when the tissue becomes fully coagulated, *i.e.*,  $c(t) \rightarrow 0$ . The more practical measure of the damage degree used here is the relative fraction change of the undamaged tissue:  $\Omega_1 = [c(0) - c(t)]/c(0) = 1 - \exp(-\Omega)$ . The latter parameter is always positive and never exceeds unity. Clearly,  $\Omega_1 = 0$  indicates the absence of damage while  $\Omega_1 = 1$  means that the tissue is fully coagulated. It is worth noting that parameters  $\Omega_1$  and  $\Omega$  are very close to each other when the damage degree is small as compared to unity. The parameter values used in the simulations here were:  $A=3.1 \cdot 10^{98} \text{ s}^{-1}$  and  $E_a=6.28 \cdot 10^5$  J/mole (Pearce *et al.* (1995) In Optical-thermal response of laser-irradiated tissue eds. Welch *et al.* (NY and London: Plenum Press) pp. 561-606).

### B. Theoretical model of islet lattice relaxation.

The theory of selective photothermolysis considers the thermal relaxation time (TRT) of an individual target as the characteristic time required for an overheated target to come to the thermal equilibrium with its environment. It is suggested that the TRT is  $d^2/(8\alpha)$ ,  $d^2/(16\alpha)$ , and  $d^2/(24\alpha)$  for the planar (one-dimensional), cylindrical (two-dimensional), and spherical (three-dimensional) targets, with  $d$  being the target width (one-dimensional) or diameter (two or three-dimensional).

This definition can be extended to an islet lattice. Significantly, if the lattice is very sparse, *i.e.*, the fill factor is much smaller than 1, the LTRT can be almost equal to the TRT of an individual islet. It can be expected, however, that dense lattices will come to an equilibrium faster than the sparse ones, as well as that the LTRT will be determined predominantly by the dimensionality of the lattice, its fill factor, and the islet TRT.

A precise definition of LTRT was formulated as follows: let the islets be heated to temperature  $T_0$  at time zero with the tissue temperature in between them being  $T_b < T_0$ . If no external action occurs, the temperature gradients in the lattice will decay in time and the lattice will approach the thermal equilibrium at stationary temperature

$T_{st} = T_b + (T_0 - T_b) \cdot f$ . Since the stationary temperature cannot be reached for a finite time, the LTRT can be defined as the time needed for the islets to cool down to the intermediate temperature  $T_1 = T_{st} + (T_0 - T_{st}) \cdot e^{-1} = T_b + (T_0 - T_b) \cdot \frac{1+f \cdot (e-1)}{e}$ , with  $e$  being the natural logarithm base.

The LTRT is dependent on the lattice fill factor,  $f$ , which can be illustrated by first considering the particular case of the two-dimensional lattice. Disregarding the effect of the precise voxel and islet shapes, it can be assumed that the islet and the voxel are infinite cylinders of radii  $r_0$  and  $R = r_0/\sqrt{f}$ , respectively. Apparently, the cylindrical pattern cannot be translated in space to form a lattice. However, it is unlikely that the transformation of the actual voxel into the cylinder of the same cross-sectional area can change the LTRT appreciably. The significance of this transformation is that it decreases the dimensionality of the problem to 1. The time-dependent heat equation within the cylindrical voxel was solved mathematically by applying a periodic (symmetry) boundary conditions on its outer surface.

Therefore, the heat equation, the initial condition, and the boundary conditions in the cylindrical frame can be written as follows:

$$\rho c \frac{\partial}{\partial t} T(r, t) = \frac{\kappa}{r} \frac{\partial}{\partial r} \left( r \frac{\partial}{\partial r} T(r, t) \right), \quad (\text{A12})$$

$$T(r, 0) = T_0 \cdot \begin{cases} 1, & r \leq r_0, \\ 0, & r > r_0, \end{cases} \quad (\text{A13})$$

$$\frac{\partial}{\partial t} T(0, t) = \frac{\partial}{\partial t} T(R, t) = 0, \quad (\text{A14})$$

where  $\rho$ ,  $c$ , and  $\kappa$  are the density, the specific heat, and the thermal conductivity of the tissue. It is suggested that  $T_b = 0$ , which does not limit the generality of the analysis.

Introducing the dimensionless time  $\tau = t/\text{TRT}$  and the dimensionless coordinate  $\xi = r/r_0$  (where  $\text{TRT} = d_0^2/(16\alpha) = r_0^2/(4\alpha)$  is the TRT of the cylindrical islet and  $\alpha = \kappa/(\rho c)$  is the thermal diffusivity) the following equations were obtained:

$$\frac{\partial}{\partial \tau} T(\xi, \tau) = \frac{1}{4\xi} \frac{\partial}{\partial \xi} \left( \xi \frac{\partial}{\partial \xi} T(\xi, \tau) \right), \quad (\text{A15})$$

$$T(\xi, 0) = T_0 \cdot \begin{cases} 1, & \xi \leq 1, \\ 0, & \xi > 1, \end{cases} \quad (\text{A16})$$

$$\frac{\partial}{\partial \tau} T(0, \tau) = \frac{\partial}{\partial \tau} T(\sqrt{f^{-1}}, \tau) = 0. \quad (\text{A17})$$

Equations (A15)-(A17) can be solved numerically to evaluate the LTRT, that is the time when the temperature at the voxel center reduces to  $T(0, \tau) = T_1 = T_0 \cdot \frac{f+1}{2}$ . It is worth noting that set (A15)-(A17) is linear with respect to temperature and the LTRT does not depend on the initial temperature thereof. Consequently, the ratio of the LTRT to the islet TRT depends on the lattice fill factor only. Apparently, this simplification comes from the assumptions made for reducing the dimensionality of the problem.

### C. Lattice temperature relaxation time (LTRT).

To obtain the lattices of the thermal islets (LTI), a corresponding lattice of optical islets (LOI) has to be created first. The next step is to make the pulse width short enough to avoid overlapping of the adjacent thermal islets. It should be emphasized that LTI is a time-dependent structure and the latter requirement implies that the islets should not overlap at the time instant when the temperature reaches its maximum.

The limitation on the pulse width may be specified in the context of the theory of selective photothermolysis (Anderson *et al.* (1983), *Science* 220: 524-26; Altshuler *et al.* (2001), *Lasers in Surgery and Medicine* 29: 416-32). In its original formulation this theory deals with isolated targets inside tissue. It points out that the selective heating of a target is possible if the pulse width is smaller than some time interval characteristic for the target and referred to as the temperature relaxation time (TRT). The TRT, in essence, is the cooling time of the target, which is the time required by an instantly heated target to cool to 1/e of its initial temperature. This concept is applicable easily to the individual islets. It may be pointed out that the TRT of the planar islet (layer of the tissue, one-dimensional) is  $d^2/(8\alpha)$  with  $d$  and  $\alpha$  being the target width and the thermal diffusivity of the tissue, respectively. For the cylindrical (two-dimensional) and spherical (three-dimensional) targets the corresponding relations read:  $d^2/(16\alpha)$  and  $d^2/(24\alpha)$  with  $d$  being the islet diameter (Altshuler *et al.* (2001), *Lasers in Surgery and Medicine* 29: 416 – 32). This concept was generalized to periodic lattices of the optical islets as discussed below.

It is postulated that the lattice temperature dynamics depends on the relation between the islet and voxel areas rather than by the precise islet and voxel shapes. This

should be valid if the voxels are not very anisotropic, *i.e.*, long in one direction and short in the others. The anisotropic lattices, in turn, may be considered as the lattices of smaller dimensionality. In particular, the lattice dimensionality is reduced from 2 to 1 if the voxels are very long and narrow rectangles: it is possible to switch from such rectangles to the infinitely long stripes of the same width making up a one-dimensional lattice.

Thermal dynamics of LTI depends on the method of the LOI introduction into the skin. First method is a “sequential method” or “sequential LOP”. In this case in every time instant just one (or several distant) optical islet is being created in the tissue. Laser beam scanners can be used to create sequential LOI. Second method is “parallel method” or “parallel LOP”. In this case, a multitude of optical islets are created in the tissue simultaneously during the optical pulse. Thermal interaction between islets in the sequential LOI is minimal. For parallel LOI, thermal interaction between different islets can be very significant. To evaluate the lattice thermal relaxation time (LTRT), for parallel LOI, the same reasoning used to find the TRT of an individual islet is followed. The islets are heated instantly to temperature  $T_0$  keeping the space outside them at the constant background temperature  $T_b < T_0$ . By letting the islets cool through the conduction of heat to the surrounding tissue, the lattice will approach thermal equilibrium at the stationary temperature

$$T_{st} = T_b + (T_0 - T_b) \cdot f, \quad (A22)$$

which depends on the fill factor. The LTRT may be defined as the characteristic cooling time when the islet temperature (more precisely, the maximum temperature within the islet) reaches the intermediate value between the initial and stationary temperatures:

$$T_1 = T_{st} + (T_0 - T_{st}) \cdot e^{-1} = T_b + (T_0 - T_b) \cdot \frac{1 + f \cdot (e - 1)}{e}. \quad (A23)$$

Using this definition the LTRT of a very sparse lattice equals the TRT of an individual islet. For such a lattice each islet cools independently on the others. For denser lattices, however, the temperature profiles from different islets overlap causing the LTRT to decrease. This cooperative effect was studied by evaluating the LTRT to TRT ratio as a function of the fill factor for the particular case of the lattice of the cylindrical islets, as described herein. The LTRT decreases monotonically with the growth of the fill factor. Therefore, the denser is the islet lattice the smaller is the time while the lattice relaxes by coming down to the thermal equilibrium with the surrounding tissue. When the fill factor approaches unity, the LTRT approaches some limit close but somewhat larger than the TRT. The distinction is due to some disagreement between the definition of LTRT used here and the conventional definition of TRT. The real temperature decay is not exponential due to the heating of the surrounding tissues. Therefore, the time necessary for the target to decrease its temperature to  $1/e$  of its initial value is always larger than TRT and this time is the actual upper limit of LTRT (the LTRT approaches this limit when the fill factor is zero).

As a rough estimate of the dependence of the LTRT to TRT ratio on the fill factor, a simple relation may be used:

$$\frac{\text{LTRT}}{\text{TRT}} \approx \frac{1}{3 \cdot f}, \quad (\text{A24})$$

providing a good fit of the numeric data for  $f > 0.1$ . Actually, equation (A24) means that the LTRT is proportional to the time interval,  $\Delta^2/(2 \cdot \alpha)$ , while the heat front covers the distance between the islets  $\Delta = d/\sqrt{f}$ . If the voxel size is very large compared to the islet diameter, the contrast of the thermal lattice may become small before the heat front covers distance  $\Delta$ . Therefore, equation (A24) overestimates the LTRT appreciably if  $f < 0.1$ .



D. Light fluence parameters for islet formation in a tissue.

In order to get isolated islets, the incident fluence has to be bounded from both above and below:  $F_{\min} < F < F_{\max}$ . The meaning of the latter expression is that the fluence has to be large enough to provide the desired effect within the islets but should be insufficient to cause the same effect in the whole bulk of the tissue. Practically, the right-hand-side inequality is sufficient to avoid the bulk effect in all cases while the left-hand-side warrants the formation of the islets only if the pulse width is rather short so that the relation between the delivered light energy and the attained effect is local. This means that the effect depends on the total irradiance at the same point of the tissue rather than on the average irradiance over some area. For the longer pulses, however, the dependence may become non-local due to the heat and mass transfer within the tissue (Sekins *et al.* (1990) In *Therapeutic Heat and Cold*, 4-th edition Ed. Lehmann (Baltimore: Williams & Wilkins) pp. 62-112). Therefore, the islets may not appear even if the left-hand-side inequality holds.  $F_{\min}$  can be found as a fluence needed to heat up tissue in a islet to the threshold temperature for the tissue coagulation,  $T_{tr}$ . If the pulse width is short enough to neglect the heat conduction, the threshold fluence for the protein coagulation is given by:

$$F_{\min} = \rho c (T_{tr} - T_i) / \mu_a, \quad (A18)$$

where  $\rho$  is the skin density,  $c$  is its specific heat,  $\mu_a$  is the skin absorption coefficient, and  $T_i$  is the initial temperature. The threshold of the bulk damage  $F_{\max}$  is the fluence needed to heat up tissue, both within the islets and between the islets (bulk tissue), to the threshold temperature. Because the volume of this tissue is  $1/f$  times larger than the volume occupied by islets:

$$F_{\max} = F_{\min} / f. \quad (A19)$$

This formula is based on the assumption that the treatment is safe provided that enough intact tissue is left between the islets for assured recovery. A more conservative

assumption is that, in addition to the first criterion, the treatment is safe until the temperature in the islets reaches the threshold of thermomechanical effects,  $T_{\max}$ . In this case

$$F_{\max} = F_{\min} \cdot (T_{\max} - T_i) / (T_{tr} - T_i) \quad (A20)$$

The first criterion predicts a significant safety gap. For example, for  $f=0.25$ , the islets and spaces between them have equal safety margins,  $F_{\max}/F_{\min} = 4$ . The second criterion is more restrictive. For skin,  $T_{\max}$  can be determined as the temperature of vaporization of water  $T_{\max} = 100^\circ\text{C}$ . Protein coagulation temperature for ms range pulse width is  $T_{tr} = 67^\circ\text{C}$  and the second criterion yields the safety margin  $F_{\max}/F_{\min} = 2.1$ .

A large safety margin is one of the most important features of the lattice approach. The above estimate of safety is true for periodical (regular) lattices. If lattice is irregular, islets can overlap and create large area of damage. It is the main reason why later analysis is focused on regular lattices.

Isolated islets are considered before the islet lattices. A typical method of creating a 3-dimensional (three-dimensional) optical islet is focusing light inside the skin. The optical islet of a high contrast may be obtained if the numerical aperture (NA) of the input beam is sufficiently large. However, if the NA is too large one may expect trapping and waveguide propagation of light in epidermis, which has a higher index of refraction than the underlying dermis.

#### E. Wavelength dependency of threshold fluences.

The threshold fluences for the islet treatments  $F_{\min}$  are always wavelength dependent. The particular dependence of this kind is illustrated by Fig. 64, which shows the spatially confined thermal damage of the type II skin caused by the pulses of the collimated light of diameter 0.1 mm striking the skin surface through sapphire. The pulse width was assumed to be short enough to neglect the leakage of the heat energy out of the treatment site during the pulse (the so-called adiabatic mode). If the islet is the cylinder

of diameter  $d=0.1$  mm, the temperature relaxation time is  $TRT = d^2/(16\alpha) \approx 10$  ms, where  $\alpha \approx 10^{-3} \text{ cm}^2 \text{ s}^{-1}$  is the thermal diffusivity. The threshold light fluence was evaluated incident on the skin, which heated the tissue by  $30^\circ\text{C}$  at the characteristic depth of 0.25 mm (curve 1), 0.5 mm (curve 2) and 0.75 mm (curve 3), respectively, and coagulated tissue up to this depth. The regions of low threshold fluence in Fig. 64 correspond to the absorption peaks of the tissue water.

The region of the low threshold fluence near 970 nm coincides with the weak water absorption peak. However, other minima are shifted from the water absorption peaks and this shift is an increasing function of the depth of damage. The reason for this is that the low threshold fluence is always a compromise between the strong absorption and low attenuation of light in the skin. Minimum threshold of damage for 0.25 mm, 0.5 mm and 0.75 mm depth was observed for 1450 nm, 1410 nm, and 1405 nm, respectively. As can be seen in Fig. 64, the threshold fluence depends on depth of tissue damage. A behavior of threshold of damage spectrum  $F_{th}(\lambda)$  is similar for all depths with an exception of the 1400 – 1600 nm range. In this range, damage spectrum  $F_{th}(\lambda)$  has coinciding minima for 0.25 mm and 0.5 mm depths. For a deeper damage (0.75 mm),  $F_{th}(\lambda)$  has two minima (1405 nm and 1530 nm), which are optimum wavelengths for deeper vertical cylinder type damage islets, and one maximum (1480 nm).

The important feature of plots 1-3 in Fig. 64 is the steep decrease of the threshold fluence towards the long-wavelength side that should be attributed to the decrease of the tissue scattering coefficient. Actually, the bulk scattering that causes the narrow beam to diverge while propagating into the skin reduces the tissue irradiance. For wavelengths longer than, typically, 1200 nm the scattering coefficients of the skin layers become relatively small providing the opportunity to create the cylindrical damage islets of a perfect shape at rather low fluences. The other issue is the relationship between the minima on curves 1-3 and the absorption maxima of the tissue water.

It is instructive to compare the penetration depth spectrum of Fig. 65 with the threshold fluence spectrum of Fig. 64. The comparison suggests that deeper-penetrating wavelengths may not necessarily be optimal from the viewpoint of maximizing thermal impact. Instead, the optimal wavelength for a given depth should be selected by

maximizing the product of irradiance (at the depth of interest) and the absorption coefficient. For islet depths up to 0.75 mm it is reasonable to use wavelengths ranging from 1200 to 1800 nm, laying outside the strong absorption peaks of water and providing relatively low scattering of light in the tissue.

For treatment at superficial (up 0.75 mm) depth collimated beam with diameter around 0.1 can be effectively used to form LOL. To prevent stratum corneum and epidermis from damage, wavelengths with high absorption by water (around 1.45, 1.9  $\mu\text{m}$ ) can be used to take advantages of the low water content in stratum corneum and epidermis vs. dermis. Additionally, selective cooling of stratum corneum and epidermis can be employed. For deeper targets in the dermis and hypodermis, large sizes of optical islets have to be used.

#### F. Formation of optical islets using the focusing method.

Fig. 66 illustrates the formation of the three-dimensional optical islets by the focusing method. It shows the calculated distribution of the skin irradiance on the axis of the uniform beam focused inside the type II skin (Fitzpatrick (1998), *Arch. Dermatol.* 124: 869-71) to the depth of 0.5 mm. The beam diameter is 1 mm so that its numerical aperture is 1. The skin irradiance was normalized to the input light fluence at the skin/sapphire boundary. Curves 1 through 6 were obtained for the specified wavelengths using the four-layer skin model described in this invention. Each curve demonstrates a sharp peak at the focusing depth - the so-called ballistic focus. This peak broadens due to multiple scattering of light on the microscopic skin heterogeneities like cell membranes, mitochondria, cell nuclei, etc. The ballistic focus itself is formed by a small portion of photons reaching the focusing depth without scattering. The contribution of the ballistic photons into the total energy balance is very small; however, these photons are concentrated in a tiny area around the focusing point forming the sharp peak of irradiance. The size of the latter area and, therefore, the height of the ballistic peak are determined by the aberrations of the ballistic light due to the macroscopic changes of the skin refraction index. The skin model described here uses different refraction indices for different layers and postulates the planar layer boundaries. Real layer boundaries are curved yielding larger aberrations than the plane boundaries. Therefore, this model may

overestimate the height of the ballistic peak. The other issue is the size of the mesh elements used in the Monte-Carlo simulations. Actually, the Monte-Carlo routine of this invention evaluates the average irradiance within the voxel rather than the local irradiance at a certain point. The size of mesh elements used here was 10  $\mu\text{m}$  in both directions. Smaller elements were not used because the light transport theory does not describe the microscopic oscillations of the irradiance and the voxel size has to be much larger than the wavelength.

The majority of incident photons undergo multiple scattering and do not contribute to the ballistic peak itself. However, light scattering is highly anisotropic in the NIR range. This means that the direction of the scattered photon is strongly correlated with its initial direction. For this reason, the irradiance distribution formed by the scattered light may be somewhat close to that formed by the ballistic light. Particularly, a high peak of scattered irradiance may appear around the focusing point being much wider than the ballistic peak and involving much more light energy. The composite (ballistic plus scattered) peak around the focusing point is called the “geometrical focus”. The magnitude of the irradiance maximum in the focus becomes small if the scattering coefficient is too large for a particular wavelength or the focusing is too deep.

#### G. Relationship between irradiance and focus depth.

The maximum of irradiance around the focusing point decreases gradually with the increase of the focusing depth. Simultaneously, a wide peak of irradiance appears above the focusing point. The latter peak may be called “diffused focus”. This is illustrated by Fig. 67 where focusing of the 1064 nm light to depths 0.5 (1), 0.6 (2), 0.7 (3), and 1 (4) mm inside the skin through sapphire is analyzed. In the latter case, the geometrical focus can hardly be recognized whereas the “diffused” one is clearly seen.

The irradiance profile inside the skin is determined by the two competing processes: the geometrical convergence and the divergence through the multiple scattering of light in the bulk tissue. The scattering coefficient decreases gradually with the increase of the wavelength.

#### H. Monte-Carlo simulations of light transport.

The plane or cylindrical optical islets perpendicular to the skin surface may be obtained by using a narrow collimated light beam in the skin. A beam is considered collimated in the skin if it neither converges nor diverges in a non-scattering space with the refractive index matching that of skin at the depth of treatment  $z_0$ . Minimal diameter of collimated beam can be found from the formula (Yariv (1989) Quantum Electronics (NY: John Wiley and Sons)):

$$d_{\min} = 5(z_0 \lambda / \pi)^{1/2}, \quad (\text{A21})$$

where  $\lambda$  is the wavelength. For typical depth  $z_0=1$  mm and  $\lambda=1500$  nm,  $d_{\min}=0.1$  mm. The spot profile may be a line (stripe) for the one-dimensional islet and some limited shape like circle or square for the two-dimensional islet. For a circular optical beam (wavelength 1200 nm) of diameter 100  $\mu\text{m}$  striking the skin through sapphire, the transverse intensity profile of the beam is flat at small depths and transfers to a Gaussian when moving deeper into the skin. Therefore, the optical islet is a cylinder very sharp at the top and somewhat blurred at the bottom. It will be demonstrated below that the weak irradiance outside the original cylinder may not contribute to the tissue damage provided the pulse is short enough. This opens the opportunity of creating the damage islets of a very precise cylindrical shape.

#### I. Effects of beam diameter and wavelength on penetration depth.

To evaluate the shape of an islet it is important to account for an effect of beam diameter on the penetration depth of light into the skin. The penetration depth is defined as the depth into the tissue where the irradiance is  $1/e$  of the fluence incident onto the skin surface. This effect is well studied for beams wider than, typically, 1 mm (Klavuhn (2000) Illumination geometry: the importance of laser beam spatial characteristics Laser hair removal technical note No 2 (Published by Lumenis Inc)). However, if the beam is only several tens of micrometers in diameter, which is much smaller than the diffuse length of light in the skin, the propagation dynamics may be very different from that of

wider beams. In particular, for such narrow beams the irradiance decreases monotonically when moving deeper into the skin along the beam axis whereas for the wider beams a subsurface irradiance maximum may occur. This is illustrated by Fig. 68, where plots 1 and 2 are for wide (diameter 10 mm) and narrow (diameter 0.1 mm) beams at wavelength 1060 nm. It should be noted herewith that the total bulk irradiance in skin is the sum of the direct and scattered components and the subsurface maximum is due to the scattered component only. When the beam diameter decreases the on-axis irradiance becomes predominantly due to the direct component and the subsurface maximum disappears.

Fig. 65 shows the wavelength dependence of the penetration depth for the uniform circular beam of incident diameter 0.1 mm. The dependence appears to be rather flat in contrast to the case of the wide beam (Jacques *et al.* (1995) In Optical-thermal response of laser-irradiated tissue eds. Welch *et al.* (NY and London: Plenum Press) pp. 561-606; Jacques (1996) In Advances in Optical Imaging and Photon Migration eds. Alfano *et al.* 2: 364-71; Anderson *et al.* (1994), *Proc. SPIE* MS-102: 29-35). The maximum variation of the penetration depth in the specified range is 30-35% only. The penetration depth is limited by the water absorption and the tissue scattering. Apparently, the effect of scattering is stronger for the narrow beams than for the wide ones. The tissue scattering becomes smaller with the wavelength rise while the water absorption increases. These two effects partially compensate each other and the net variations of the penetration depth are rather small.

#### J. Dynamics of damage development.

The lattices of the damage islets develop from those of the thermal islets provided certain restrictions on the pulse width and the light flux are met. The dynamics of the damage development is governed by the Arrhenius formula. The relationship between the temperature and damage islets is not straightforward. Various tissue sites may show the same peak temperature but a different damage degree, depending on the time the temperature is maintained above the activation threshold of the coagulation reaction. Moreover, if the pulse width is small the temperature islets can become very sharp at the end of the pulse. If this is the case, the steep temperature gradients may cause the islets to extend and damage the surrounding tissue after the light is off. The effect of such

extension leads to onset of bulk damage when the fill factor increases beyond the safe limit.

The LOI technique has several fundamental differences and potential advantages vs. traditional treatment, which employs uniform optical beams for bulk tissue heating and damage. The following conclusions were reached from the computational and theoretical models of islets and islet formation:

(1) In addition to traditional parameters characterizing light treatment, such as the wavelength, the fluence, the pulse width and the spot size, two new important factors are introduced: the fill factor (fractional volume) and the size of islets. Furthermore, the resulting therapeutic effect can be influenced by the geometry (shape, symmetry) and dimensionality of the lattice and islets. LOI can be introduced at different depths at the tissue. For example, in the skin LOI can be localized in stratum corneum, epidermis, dermis, or hypodermis. For deep LOI, focusing technique and selective superficial cooling can be used. A suitable range of wavelengths for the LOI treatment is the near-infrared range (900 – 3000 nm), with water serving as the main target chromophore.

(2) The main potential advantage of the LOI approach vs. the traditional one is a significantly higher safety margin between the threshold of therapeutic effect and the threshold of unwanted side effects. The safety margin is defined as  $F_{\max} / F_{\min}$ , where  $F_{\min}$  is the threshold of the desired therapeutic effect and  $F_{\max}$  is the threshold of the continuous bulk damage. The theoretical upper limit for the safety margin is  $1/f$ , where  $f$  is the fill factor of the lattice. Practically, the safety margin is determined by the expression  $F_{\max} = F_{\min} \cdot (T_{\max} - T_i) / (T_{tr} - T_i)$ , where  $T_{\max}$  is the temperature of water vaporization,  $T_{tr}$  is the minimal temperature, which still provides the therapeutic effect. This margin can be up to 2 times higher than in case of traditional photothermal treatment. It should also be emphasized that the periodicity of the lattice is important for keeping the safety margin stable and for maintaining reproducibility of results.

(3) The efficacy of the lattice treatment can be increased by minimizing the size of the islets and maximizing the fill factor of the lattice. Small-size spherical or elliptical islets can be produced by using wavelengths in the 900 to 1800 nm range and focusing technique with a high numerical aperture for depth in the skin up to 0.7 mm with minimal irradiation of epidermis. The positions of the optical islets correspond to the locations of



ballistic foci. For deeper focusing, the ballistic focus disappears and the maximal irradiance stabilizes at  $\sim 0.5$  mm depth (the diffuse focus).

(4) Small size column-like islets can be created in the tissue using collimated micro beams. The confocal parameter of such a beam must be longer than the depth of column in the tissue. For depths exceeding 0.5 mm, the diameter of the micro beam is generally larger than 0.1 mm. In contrast with broad beams, the depth of penetration of the micro beams is relatively insensitive to the wavelength in the range 800 -1800 nm. However, the threshold fluence for tissue damage depends strongly on the wavelength. The minimal threshold fluences can be found in the range between 1380 and 1570 nm. The depth of the resulting column can be controlled by the fluence. For a superficial column with 0.25 to 0.5 mm depth, the minimal threshold fluence can be achieved in the 1400 -1420 nm wavelength range and the absolute value of this fluence is between 12 and 80 J/cm<sup>2</sup>. For a deeper-penetrating column of a 0.75 mm depth, the minimal threshold fluences are found at 1405 nm (400 J/cm<sup>2</sup>) and 1530 nm (570 J/cm<sup>2</sup>). In principle, a LOI can be created at a depth up to several millimeters in tissue, but in this case the size of the islets will also grow to several millimeters.

(5) The extent of the optical damage is determined by the size of the optical islets and the fluence. A damage islet is collocated with the original optical islet if the pulse width is shorter than the thermal relaxation time of the optical islet and the fluence is close to the minimal effective fluence. For higher fluences, the damage islets can grow in size even after termination of the optical pulse and, as a result, the fill factors of LTI and LDI can be higher than the fill factor of the original LOI. Islets of a lattice can be created in tissue sequentially using scanner or concurrently using lattice of optical beams. In the latter case, the optimal pulse width is shorter than the thermal relaxation time of the lattice, approximately given by  $LTRT = TRT/3f$ , where  $LTRT$  and  $TRT$  are the thermal relaxation times of the LOI and a single islet, respectively.

The concept of the lattices of optical islets can be used as a safe yet effective treatment modality in dermatology, dentistry, ophthalmology, and other biomedical applications where the target of treatment is sufficiently superficial. The same concept can be applied for other sources of energy such as microwave, radiofrequency, ultrasound, and others.

## EXAMPLE 2

### Devices and Systems for Creation of Islets

One embodiment of the invention was described above in connection with Figures 3A and 3B. The following types of lenses and other focusing optics can be used with such an embodiment.

### Lenses and Other Focusing Elements.

Figs. 19A-27C illustrate various systems for delivering radiation in parallel to a plurality of target portions 214. The arrays of these figures are typically fixed focus arrays for a particular depth  $d$ . This depth may be changed either by using a different array having a different focus depth, by selectively changing the position of the array relative to the surface of the patient's skin or to target volume  $V$  or by controlling the amplitude-phase distribution of the incident radiation. Figs. 28-31 show various optical lens arrays which may be used in conjunction with the scanning or deflector systems of Figs. 32A-37 to move to successive one or more focused portions 214 within target volume  $V$ . Finally, Figs. 38 and 39 show two different variable focus optical systems which may, for example, be moved mechanically or manually over the patient's skin to illuminate successive portions 214 thereon.

#### A. Focusing elements

Figs. 19A-C show a focusing element 1 on a substrate 3, the focusing element having a border which is in a hexagonal pattern (Fig. 19A), a square pattern (Fig. 19B), and a circular or elliptical pattern (Fig. 19C). Standard optical materials can be used for these elements. While the hexagonal and square patterns of Figs. 19A and 19B can completely fill the working area of the focusing element plate 4, this is not true for the element pattern of Fig. 19C. Radiation from source 210 would typically be applied simultaneously to all of the focusing elements 1; however, the radiation could also be applied sequentially to these elements by use of a suitable scanning mechanism, or could be scanned in one direction, illuminating/irradiating for example four of the elements at a time.

### B. Micro lens systems

Figs. 20A and 20B are cross-sectional views of a micro-lens system fused in a refracting material 8, for example, porous glass. The refractive index for the material of lenses 5 must be greater than the refractive index of refracting material 8. In Fig. B2, beam 11 initially passes through planar surface 10 of refracting material 8 and is then refracted both by primary surface 6 and by secondary surface 7 of each micro-lens 5, resulting in the beam being focused to a focal point 12. The process is reversed in Fig. B2A, but the result is the same. In Figs. 20C and 20D, the incident beam 11 is refracted by a primary lens surface 6 formed of the refracting material 8. Surfaces 6 and 7 for the various arrays can be either spherical or aspherical.

### C. Lenses and lens arrays in immersion materials

In Figs. 21A and 21B, the lens pieces 15 are mounted to a substrate and are in an immersion material 16. The refraction index of lens pieces 15 are greater than the refraction index of immersion material 16. Immersion material 16 can be in a gas (air), liquid (water, cryogen spray) or a suitable solid gas and liquid can be used for cooling of the skin. The immersion material is generally at the primary and secondary plane surfaces, 13 and 14, respectively. The focusing depth can be adjusted by changing the refractive index of immersion material. In Fig. 21B, the primary surface 6 and secondary surface 7 of each lens piece 15 allows higher quality focusing to be achieved. For Figs. 21C and 21D, the lens pieces 15 are fixed on a surface of a refracting material 8, the embodiment of Fig. 21D providing a deeper focus than that of Fig. 21C, or that of any of other arrays shown in Figs. 21B-21D for a given lens 15. The lens arrays shown in Figs. 21B-21D are preferred lens arrays for practicing the teachings of this invention.

### D. Fresnel lenses

Figs. 22A-D show Fresnel lens surfaces 17 and 18 formed on a refracting material 8. Changing the profile of Fresnel lens surface 17 and 18, the relationship between the radius of center 17 and ring 18 of the Fresnel surface, makes it possible to achieve a desired quality of focusing. The arrays of Figs. 22C and 22D permit a higher quality focusing to be achieved and are other preferred arrays. Surfaces 17 and 18 can be either spherical or aspherical.

### E. Holographic lenses and spatially modulated phase arrays

In Figs. 23A and 23B, the focusing of an incident beam 11 is achieved by forming a holographic lens 19 on a surface of refracting material 8. Holographic lenses 19 may be formed on either of the surfaces of refracting material 8 as shown in Figs. 23A and 23B or on both surfaces. Fig. 23C shows that the holographic material 20 substituted for the refracting material 8 of Figs. 23A and 23B. The holographic lens is formed in the volume of material 20.

Techniques other than holography can be used to induce phase variations into different portions of the incident beam and, thus, provide amplitude modulation of the output beams.

### F. Gradient lenses

In Figs. 24A and 24B, the focusing elements are formed by gradient lenses 22 having primary plane surfaces 23 and secondary plane surfaces 24. As shown in Fig. 24B, such gradient lenses may be sandwiched between a pair of refracting material plates 8 which provide support, protection and possibly cooling for the lenses.

### G. Cylindrical lenses

Figs. 25A, 25B and 25C illustrate various matrix arrays of cylindrical lenses 25. The relation of the lengths 26 and diameters 27 of the cylindrical lenses 25 can vary as shown in the figures. The cylindrical lens 25 of Figs. 25B and 25C provide a line focus rather than a spot or circle focus as for the arrays previously shown.

Figs. 26A-26D are cross-sectional views of one layer of a matrix cylindrical lens system. The incident beam 11 is refracted by cylindrical lenses 25 (Figs. 26A and 26B) or half cylinder lenses 29 (Figs. 26C and 26D) and focus to a line focus 28. In Figs. 26C and 26D, the cylindrical lenses 29 are in the immersion material 16. Primary working optical surface 30 and secondary optical working surface 31, which may be spherical or aspherical, allowing high quality focusing to be achieved. As shown in Figs. 25A-26D the line focuses for adjacent lenses may be oriented in different directions, the orientations being at right angles to each other for certain of the lenses in these figures.

In Figs. 27A, 27B and 27C, a matrix of focal spots is achieved by passing incident beam 11 through two layers of cylindrical lenses 32 and 35. Figs. 27B and 27C are

cross-sections looking in two orthogonal directions at the array shown in Fig. 27A. By changing the focal distance of primary layer lens 32, having a surface 33, and secondary lens 35, having a surface 36, it is possible to achieve a rectangular focal spot of a desired size. Primary layer lens 32 and secondary layer lens 35 are mounted in immersion material 16. Lenses 32 and 35 may be standard optical fibers or may be replaced by cylindrical lenses, which may be spherical or aspherical. Surfaces 34 and 37 can be of optical quality to minimize edge losses.

Described above optical system can be used with a pulse laser (0.1 -100 ms) to introduce simultaneously into the skin a lattice of optical islets. For example it can be an Er:glass laser (1.56 microns wavelength) or a Nd:YAG laser (1.44 microns) with fiber delivery and imaging optics to formed uniform beam before focusing elements.

#### H. One, two, and three-lens objectives

Fig. 28 shows a one-lens objective 43 with a beam splitter 38. The beam 11 incident on angle beam splitter (phase mask) 38 divides and then passes through the refracting surfaces 41 and 42 of lens 43 to focus at central point 39 and off-center point 40. Surfaces 41 and 42 can be spherical and/or aspherical. Plate 54 having optical planar surfaces 53 and 55 permits a fixed distance to be achieved between optical surface 55 and focusing points 39, 40. Angle beam splitter 38 can act as an optical grating that can split beam 11 into several beams and provide several focuses.

In Fig. 29, a two lens 43,46 objective provides higher quality focusing and numerical aperture as a result of optimal positioning of optical surfaces 41, 42 and 44. All of these surfaces can be spherical or aspherical. Optical surface 45 of lens 46 can be planar to increase numerical aperture and can be in contact with plate 54. Plate 54 can also be a cooling element as previously discussed.

Fig. 30 differs from the previous figures in providing a three-lens objective, lenses 43, 46 and 49. Fig. 31 shows a four lens objective system, the optical surfaces 50 and 51 of lens 52 allowing an increased radius of treatment area (*i.e.*, the distance between points 39 and 40).

### I. Mirror-containing optical systems

Figs. 32A, 32B and 32C illustrate three optical systems, which may be utilized as scanning front ends to the various objectives shown in Figs. 28-31. In these figures, the collimated initial beam 11 impinges on a scanning mirror 62 and is reflected by this mirror to surface 41 of the first lens 43 of the objective optics. Scanning mirror 62 is designed to move optical axis 63 over an angle  $f$ . Rotational displacement of a normal 64 of mirror 62 by an angle  $f$  causes the angle of beam 11 to be varied by an angle  $2f$ . The optical position of scanning mirror 62 is in the entrance pupil of the focusing objective. To better correlate between the diameter of scanning mirror 62 and the radius of the working surface (*i.e.*, the distance between points 39 and 40) and to increase the focusing quality, a lens 58 may be inserted before scanning mirror 62 as shown in Fig. 32B. Optical surfaces 56 and 57 of lens 58 can be spherical or aspherical. For additional aberration control, a lens 61 may be inserted between lens 58 and mirror 62, the lens 61 having optical surfaces 59 and 60.

Figs. 33A, 33B and 33C are similar to Figs. 32A, 32B and 32C except that the light source is a point source or optical fiber 65 rather than collimated beam 11. Beam 66 from point source 65, for example the end of a fiber, is incident on scanning mirror 62 (Fig. 33A) or on surface 57 of lens 58 (Figs. 33B and 33C).

### J. Scanning systems

Figs. 34A and 34B show a two mirror scanning system. In the simpler case shown in Fig. 34A, scanning mirror 67 rotates over an angle  $f_2$  and scanning mirror 62 rotates over an angle  $f_1$ . Beam 63 is initially incident on mirror 67 and is reflected by mirror 67 to mirror 62, from which it is reflected to surface 41 of optical lens 43. In Fig. 34B, to increase the numerical aperture of the focusing beam, increase work area on the skin and decrease aberration between scanning mirrors 62 and 67, an objective lens 106 is inserted between the mirrors. While a simple one-lens objective 106 is shown in this figure, more complex objectives may be employed. Objective lens 106 refracts the beam from the center of scanning mirror 67 to the center of scanning mirror 62.

In Fig. 35, scanning is performed by scanning lens 70, which is movable in direction  $s$ . When scanning lens 70 is moved to an off center position 73, optical surface 68 refracts a ray of light along optical axis 71 to direction 72.

In Fig. 36, scanning is performed by rotating lens 76 to, for example, position 77. Surface 74 is planar and surface 75 is selected so that it does not influence the direction of refracted optical axis 72. In Fig. 37, scanning is performed by the moving of point source or optical fiber 65 in directions.

#### K. Zoom lens objectives

Figs. 38 and 39 show zoom lens objectives to move the damage islets to different depths. In Fig. 38, a first component is made up of a single lens 81 movable along the optical axis relative to a second component, which is unmovable and consists of two lenses 84 and 87. Lens 84 is used to increase numerical aperture. To increase numerical aperture, range of back-focal distance and decrease focal spot size, optical surfaces 79, 80, 82, 83 and 85 can be aspherical. The relative position of the first and second components determines the depth of focal spot 12.

Fig. 39 shows zoom lens objectives with spherical optical surfaces. The first component is made up of a single lens 90 movable with respect to the second component along the optical axis. The second component, which is unmovable, consists of five lenses 93, 96, 99, 102, and 105. The radius of curvature of surfaces 88 and 89 are selected so as to compensate for aberrations of the unmovable second component. Again, the depth of focus may be controlled by controlling the distance between the first and second components. Either of the lens systems shown in Figs. 38 and 39 may be mounted so as to be movable either manually or under control of control 218 to selectively focus on desired portions 214 of target volume V or to non-selectively focus on portions of the target volume.

#### L. Focus Depth.

While as may be seen from Table B1, depth  $d$  for volume V and the focal depth of optical system 212 are substantially the same when focusing to shallow depths, it is generally necessary in a scattering medium such as skin to focus to a greater depth, sometimes a substantially greater depth, in order to achieve a focus at a deeper depth  $d$ . The reason for this is that scattering prevents a tight focus from being achieved and results in the minimum spot size, and thus maximum energy concentration, for the focused beam being at a depth substantially above that at which the beam is focused. The

focus depth can be selected to achieve a minimum spot size at the desired depth  $d$  based on the known characteristics of the skin.

#### M. Wavelength.

Both scattering and absorption are wavelength dependent. Therefore, while for shallow depths a fairly wide band of wavelengths can be utilized while still achieving a focused beam, the deeper the focus depth, the more scattering and absorption become factors, and the narrower the band of wavelengths available at which a reasonable focus can be achieved. Table B1 indicates preferred wavelength bands for various depths, although acceptable, but less than optimal, results may be possible outside these bands.

**Table B1**

| Depth of damage, $\mu\text{m}$ | Wavelength range, nm  | NumericalAperture range |
|--------------------------------|-----------------------|-------------------------|
| 0-200                          | 290 - 10000           | <3                      |
| 200-300                        | 400-1880 & 2050-2350  | <2                      |
| 300-500                        | 600--1850 & 2150-2260 | <2                      |
| 500-1000                       | 600-1370 & 1600-1820  | <1.5                    |
| 1000-2000                      | 670-1350 & 1650-1780  | <1                      |
| 2000-5000                      | 800-1300              | <1                      |

#### N. Pulse Width.

Normally the pulse width of the applied radiation should be less than the thermal relaxation time (TRT) of each of the targeted portions or optical islets 214, since a longer duration will result in heat migrating beyond the boundaries of these portions. Since the portions 214 will generally be relatively small, pulse durations will also be relatively short. However, as depth increases, and the spot sizes thus also increase, maximum pulse width or duration also increase. The pulse-widths can be longer than the thermal relaxation time of the target portion 214 if density of the targets is not too high, so that the combined heat from the target areas at any point outside these areas is well below the damage threshold for tissue at such point. Generally, thermal diffusion theory indicates that pulse width  $\tau$  for a spherical islet should be  $\tau < 500 D^2/24$  and the pulse width for a cylindrical islet with a diameter  $D$  is  $\tau < 50 D^2/16$ , where  $D$  is the characteristic size of the



target. Further, the pulse-widths can sometimes be longer than the thermal relaxation time of the target portion 214 if density of the targets is not too high, so that the combined heat from the target areas at any point outside these areas is well below the damage threshold for tissue at such point. Also, as will be discussed later, with a suitable cooling regimen, the above limitation may not apply, and pulse durations in excess of the thermal relaxation time for a damage portion 214, sometimes substantially in excess of TRT, may be utilized.

#### O. Power.

The required power from the radiation source depends on the desired therapeutic effect, increasing with increasing depth and cooling and with decreasing absorption due to wavelength. The power also decreases with increasing pulse width.

#### P. Cooling.

Typically cooler 215 is activated before source 210 to pre-cool the patient's skin to a selected temperature below normal skin temperature, for example  $-5^{\circ}\text{C}$  to  $10^{\circ}\text{C}$ , to a depth of at least DE junction 206, and preferably to depth d to protect the entire skin region 220 above volume V. However, in accordance with the teachings of this invention, if pre-cooling extends for a period sufficient for the patient's skin to be cooled to a depth below the volume V, and in particular if cooling continues after the application of radiation begins, then heating will occur only in the radiated portions 214, each of which portions will be surrounded by cooled skin. Therefore, even if the duration of the applied radiation exceeds TRT for portions 214, heat from these portions will be contained and thermal damage will not occur beyond these portions. Further, while nerves may be stimulated in portions 214, the cooling of these nerves outside of portions 214 will, in addition to permitting tight control of damage volume, also block pain signals from being transmitted to the brain, thus permitting treatments to be effected with greater patient comfort, and in particular permitting radiation doses to be applied to effect a desired treatment which might not otherwise be possible because of the resulting pain experienced by the patient. This cooling regimen is an important feature of this invention.

Q. Numerical Aperture.

Numerical aperture is a function of the angle  $\theta$  for the focused radiation beam 222 from optical device 212. It is preferable that this number, and thus the angle  $\theta$ , be as large as possible so that the energy at portions 214 in volume V where radiation is concentrated is substantially greater than that at other points in volume V (and in region 220), thereby minimizing damage to tissue in region 220, and in portions of volume V other than portions 214, while still achieving the desired therapeutic effect in the portions 214 of volume V. Higher numerical aperture of the beam increases safety of epidermis, but it is limited by scattering and absorption of higher incidence angle optical rays. As can be seen from Table B1, the possible numerical aperture decreases as the focus depth increases.

EXAMPLE 3Enhanced-Penetration Channels and Optical Clearance of Pig Skin *In Vitro*

A lattice of damage islets was created in the stratum corneum of farm pig skin using a standard flash-arc-lamp system that emits in the 650-1200 nm band (StarLux Rs™, Palomar Medical Technologies, Burlington, MA) and a damage islet mask consisting of carbon particles in a film which was applied to the surface of the skin. Furthermore, to determine optical clearance of treated areas of pig skin specimens, a 40% solution of glucose in water was applied to the surface of the specimen. Optical clearance refers to a change in optical properties of the tissue which makes it more transparent in the optical range by reducing light scattering. Permeation of the skin by glucose or glycerin increases the optical clearance by reducing the refractive index differences between the interstitial solution and the intercellular matrix proteins collagen and elastin.

In a first set of experiments, an approximately 4 cm<sup>2</sup> farm pig skin specimen was glued (LOCTITE 411 glue) to a rigid transparent substrate and cleaned with an alcohol wipe. The dry skin surface was divided into four 1 cm<sup>2</sup> areas. A damage islet mask was placed on the surface of the specimen and covered with a thin layer of lotion (LuxLotion™, Palomar Medical Technologies, Burlington, MA) to improve optical coupling to the light source. Two of the four 1 cm<sup>2</sup> areas of the specimen received two

pulses (duration 20 ms) at  $36 \text{ J/cm}^2$  using the StarLux Rs hand piece. One  $1 \text{ cm}^2$  area of the specimen received two pulses (duration 10 ms) at  $20 \text{ J/cm}^2$ . The fourth  $1 \text{ cm}^2$  area of the specimen served as a non-treated control. The distances between the treated areas were approximately 1 cm. After treatment, loose carbon particles on the surface were removed, and the specimen was covered with 40% solution of glucose, and kept warm using a hair dryer. The surface of the sample was kept wet by adding fresh glucose solution.

Thin blue wires were placed under the test areas of the specimen after the treatment, and optical clearance of the tissue was assessed by observation of visual appearance of blue wires through the specimen.

The skin specimen was photographed before the treatment (Figure 52), immediately after the treatment, and every 15 min for 75 min after the treatment. Carbon particles were removed after the treatment, and the cleaned sample was photographed.

The lattice of damage islets procedure described above created damage islets in the stratum corneum of the farm pig skin specimen that were barely noticeable (Figure 53). Maximum optical clearance was observed 60 min after the  $36 \text{ J/cm}^2$  light pulses (20 ms). The  $36 \text{ J/cm}^2$  (20 ms) pulses achieved noticeably better clearance than the  $20 \text{ J/cm}^2$  (10 ms) pulses. No detectable clearance was observed in the control (non-treated) area of specimen. (See Figure 54).

A lattice of thermal damage islets was created in the stratum corneum of the farm pig skin specimen *in vitro*. The thermal damage islets (*i.e.*, enhanced permeability paths) allowed for superior permeation of the skin by topically applied glucose as evidenced by significantly higher optical clearance than non-treated areas.

In a second set of experiments, an approximately  $4 \text{ cm}^2$  farm pig skin specimen was glued to a rigid transparent substrate and cleaned with alcohol wipe, and a damage islet mask was placed on the surface of the specimen and covered with a thin layer of lotion, as described above. Two adjacent, approximately  $1 \text{ cm}^2$  areas of specimen received one pulse of  $36 \text{ J/cm}^2$  for 20 ms. Carbon particles were removed after treatment, and the specimen was covered with a 40% solution of glucose in water and maintained at the room temperature for 1 hr. The specimen was warmed up to approximately  $40^\circ\text{C}$  for 2-3 min twice during this period. After one hour, one of the treated areas received two

additional pulses of 20 ms at 36 J/cm<sup>2</sup>. Carbon particles were removed and specimen was covered with 40% glucose solution and kept warm using a hair dryer. The surface of the sample was kept wet with fresh glucose solution as needed. Approximately two hours after treatment, optical clearance was assessed by visual observation and documented by photography (see Figures 55 and 56).

The specimen area treated with three pulses (20 ms) at 36 J/cm<sup>2</sup> showed total optical clearance, as compared to no clearance of the non-treated area. The specimen area treated with one pulse (20 ms) at 36 J/cm<sup>2</sup> showed only partial optical clearance, as compared to no clearance of the non-treated area.

#### Enhanced Penetration Channels and Optical Clearance of Human Skin *In Vivo*

A lattice of damage islets was created in the stratum corneum of a human subject *in vivo* using a flash-arc-lamp system (StarLux Rs™, Palomar Medical Technologies, Burlington, MA) and a damage islet mask, as described above. Furthermore, to determine optical clearance of treated areas of skin specimens, a 40% solution of glucose in water was applied to the surface of the specimen.

A tattoo site on a subject's right leg was cleaned with an alcohol wipe and dried. The skin area pre-treatment was photographed (Figure 57). A flash-arc-lamp system hand piece aperture was covered with a thin layer of lotion (LuxLotion™, Palomar Medical Technologies, Burlington, MA) and laser treatment was applied to the selected skin area through the damage islets mask.

A pain tolerance test was performed by applying a series of pulses with incrementally increasing fluence to a selected skin site. The damage islets mask was placed on a dry skin surface and covered with a thin layer of lotion. The pain tolerance test was performed at both the tattooed and non-tattooed sites, and the maximum tolerated fluences were used for the treatments. Two pulses (10 ms) at 10 J/cm<sup>2</sup>, two pulses (10 ms) at 18 J/cm<sup>2</sup>, and two pulses (20 ms) at 24 J/cm<sup>2</sup> were tested at the tattoo area. Two pulses (20 ms) at 24 J/cm<sup>2</sup>, two pulses (20 ms) at 30 J/cm<sup>2</sup> and three pulses (20 ms) at 36 J/cm<sup>2</sup> were tested at the tattooed and non-tattooed skin areas.

Two different tattoo sites of skin were treated with two pulses (10 ms) at 18 J/cm<sup>2</sup> two pulses (20 ms) at 24 J/cm<sup>2</sup>. Three different non-tattooed skin sites were treated with two pulses (20 ms) at 30 J/cm<sup>2</sup>, two pulses (20 ms) at 24 J/cm<sup>2</sup> and three pulses (20 ms)

at 36 J/cm<sup>2</sup>. (See Figure 58). The selected skin sites were cleaned with alcohol wipes and photographed after each treatment.

The subject's tattooed skin area was covered with one layer of a dressing sponge soaked with a 40% solution of glucose in water and kept warm using a hair dryer. The dressing sponge was kept wet by adding fresh glucose solution every 1-2 min, and was replaced every 5 min. The treated area was photographed every 15 min for 90 min. Optical clearance and stratum corneum islets were assessed by visual observation using an optical magnifier.

The subject was provided with glycerin cream for treatment of the tested area. Photos of the treated skin site were taken 6, 9, 24 and 48 hours post treatment. After 48 hours, the skin area was again covered with one layer of dressing sponge, wet with 40% solution of glucose in water, and kept warm by using hair dryer. As before, the dressing sponge was kept wet by adding fresh glucose solution every 1-2 min, and was replaced every 5 min. The treated area was photographed every 20 min for 60 min. Optical clearance and stratum corneum islets were assessed by visual observation using optical magnifier.

The lattice of damage islets procedure describe above created noticeable damage islets on the stratum corneum of the non-tattooed skin site of the subject after both two pulses (20 ms) at 30 J/cm<sup>2</sup>, and three pulses (20 ms) at 36 J/cm<sup>2</sup> (Figures 59A and 59B). The tattooed area did not show any notable damage islets 90 min after exposure (Figures 59C and 59D). No significant optical clearance was observed at any treated areas at the 90 min time point.

At the 6, 9, 24 and 48 hour time points, the lattice of damage islets became more detectable. The tattooed skin sites became clearly defined at 6 hours after exposure (Figure 60), and the area treated with three pulses (20 ms) at 36 J/cm<sup>2</sup> developed edema (Figure 61).

At the 48 hour post-treatment time point, the area treated with three pulses (20 ms) at 36 J/cm<sup>2</sup> was more red (Figure 62). The redness was interpreted as enhanced optical clearance due to the application of glycerin cream by the subject, and increased visibility of the vasculature of the dermis. Treatment of the skin site with 40% glucose

solution 48 hours after the EMR treatment did not cause any further improvement in optical clearance.

The lattice of damage islets procedure employing three pulses (20 ms) at  $36 \text{ J/cm}^2$  for normal skin and two pulses (20) at  $24 \text{ J/cm}^2$  ms for tattooed skin demonstrated a good pain tolerance margin. The method created visually noticeable damage islets *in vivo* at the selected human skin areas, and the damage islets became more defined over 6 hours. Treatment of damaged islets on human skin *in vivo* with a glycerin cream of the site subjected to three pulses (20 ms) at  $36 \text{ J/cm}^2$  resulted in optical clearance manifested by increased visibility of the dermal vasculature.

#### EXAMPLE 4

##### Devices and Systems for Producing Islets of Treatment

A number of different devices and structures can be used to generate islets of treatment in the skin. Figure 40 illustrates one system for producing the islets of treatment on the skin 280. An applicator 282 is provided with a handle so that its head 284 can be near or in contact with the skin 280 and scanned in a direction 286 over the skin 280. The applicator 282 can include an islet pattern generator 288 that produces a pattern of areas of enhanced permeability in the SC or arrangement 290 of islets particles 292 on the surface of the skin 280, which when treated with EMR from applicator 210 produces a pattern of enhanced permeability. In other embodiments, the generator 288 produces thermal, damage or photochemical islets into the epidermis or dermis.

In one embodiment, the applicator 282 includes a motion detector 294 that detects the scanning of the head 284 relative to the skin surface 296. This generated information is used by the islet pattern generator 288 to ensure that the desired fill factor or islet density and power is produced on the skin surface 296. For example, if the head 284 is scanned more quickly, the pattern generator responds by imprinting islets more quickly. The following description describes this embodiment of the invention, as well as other embodiments, in greater detail. Further, the following sections elaborate on the types of EMR sources that can be used with the applicator 282 and on the methods and structures that can be used to generate the islets of treatment.

#### A. Hand piece with diode laser bar

Some embodiments of the invention use one or more diode laser bars as the EMR source. Because many photodermatology applications require a high-power light source, a standard 40-W, 1-cm-long, cw diode laser bar can be used in some embodiments. Any suitable diode laser bar can be used including, for example, 10-100 W diode laser bars. A number of types of diode lasers, such as those set forth above, can be used within the scope of the invention. Other sources (*e.g.*, LEDs and diode lasers with SHG) can be substituted for the diode laser bar with suitable modifications to the optical and mechanical sub-systems.

Figure 12A shows one embodiment of the invention using a diode laser bar. Many other embodiments can be used within the scope of the invention. In this embodiment, the hand piece 310 includes a housing 313, a diode laser bar 315, and a cooling or heating plate 317. The housing 313 supports the diode laser bar 315 and the cooling or heating plate 317, and the housing 313 can also support control features (not shown), such as a button to fire the diode laser bar 315. The housing 313 can be made from any suitable material, including, for example, plastics. The cooling plate, if used, can remove heat from the patient's skin. The heating plate, if used, can heat the patient's skin. The same plate can be used for heating or cooling, depending on whether a heat source or source of cooling is applied to the plate.

The diode laser bar 315 can be, in one embodiment, ten to fifty emitters (having widths of 50-to-150  $\mu\text{m}$  in some embodiments or 100-to-150  $\mu\text{m}$  in others) that are located along a 1-cm long diode bar with spacing of 50 to 900  $\mu\text{m}$ . In other embodiments, greater than or less than fifty emitters can be located on the diode laser bar 315, the emitter spacing, and the length of the diode laser bar 315 can also vary. In addition, the width of the emitters can vary. The emitter spacing and the number of emitters can be customized during the manufacturing process.

The diode laser bar 315 can be, in one embodiment, twenty-five 100-to-150  $\mu\text{m}$  or 50-to-150  $\mu\text{m}$  wide emitters that are located along a 1 cm long diode bar, each separated by around 50 to 900 microns in some embodiments, and approximately 500 microns in others. Figures 17 and 18 depict top and cross-sectional views, respectively, of such a diode laser bar assembly in this embodiment. In this embodiment, twenty-five emitters

702 are located directly beneath the surface plate 704 that is placed in contact with the skin during treatment. Two electrodes 706 are located to each side of the emitters 702. The bottom of the diode assembly contains a cooling agent 708 to control the diode laser and plate 704 temperatures.

In the embodiment of Figures 17 and 18, the divergence of the beam emanating from the emitters 702 is between 6 and 12 degrees along one axis (the slow axis) and between 60 and 90 degrees along the fast axis. The plate 704 may serve as either a cooling or a heating surface and also serves to locate the emitters 702 in close and fixed proximity to the surface of the tissue to be treated. The distance between the emitters 702 and the plate 704 can be between about 50 and 1000 micrometers, and more particularly between about 100 and 1000 micrometers in some embodiments, in order to minimize or prevent distortion effects on the laser beam without using any optics for low cost and simplicity of manufacture. During use, the distance between the emitters 702 and the patient's skin can be between about 50 and 1000 micrometers, and more particularly 100 and 1000 micrometers in some embodiments. In such embodiments, imaging optics are not needed, but other embodiments could include additional optics to image the emitter surfaces 702 directly onto the tissue surface. In other embodiments, greater than or less than twenty-five emitters can be located on the diode laser bar, and the length of the diode laser bar can also vary. In addition, the width of the emitters and light divergence can vary. The emitter spacing and the number of emitters can be customized during the manufacturing process.

Figure 12B shows a perspective view of one embodiment of a diode laser bar 330 that can be used for the diode laser bar 315 in Figure 12A. The diode laser bar 330 has length L of around 1 cm, a width W of around 1 mm, and a thickness T of around 0.0015 mm. The depiction of Figure 12B shows 12 emitters 332, each of which emits radiation 334 as shown in Figure 12B. The diode laser bar 330 can be placed within the device 310 of Figure 12A so that the side S of the diode laser bar 315 is oriented as shown in Figure 12A. The emitters, therefore, emit radiation downward toward the skin 319 in the embodiment of Figure 12A.

Referring again to Figure 12A, the plate 317 can be of any type, such as those set forth above, in which light from an EMR source can pass through the plate 317. In one



embodiment, the plate 317 can be a thin sapphire plate. In other embodiments, other optical materials with good optical transparency and high thermal conductivity/diffusivity, such as, for example, diamond, can be used for the plate 317. The plate 317 can be used to separate the diode laser bar 315 from the patient's skin 319 during use. In addition, the plate 317 can provide cooling or heating to the patient's skin, if desired. The area in which the plate 317 touches the patient's skin can be referred to as the treatment window. The diode laser bar 315 can be disposed within the housing 313 such that the emitters are in close proximity to the plate 317, and therefore in close proximity to the patient's skin when in use.

In operation, one way to create islets of treatment is to place the housing 313, including the diode laser bar 315, in close proximity to the skin, and then fire the laser. Wavelengths near 1750 - 2000 nm and in the 1400-1600 nm range can be used for creating subsurface islets of treatment with minimal effect on the epidermis due to high water absorption. Wavelengths in the 290-10,000 can be used in some embodiments, while in other wavelengths in the 900-10,000 nm range can be used for creating surface and subsurface islets on the skin. Without moving the hand piece across the skin, a series of treatment islets along a line can be formed in the skin. Figure 40 shows one possible arrangement 290 of islets on the surface of the skin 280 from the use of such a diode laser bar, where the diode laser bar 315 is pulsed as it moves over the skin in direction A of Figure 12A.

In another embodiment, the user can simply place the hand piece in contact with the target skin area and move the hand piece over the skin while the diode laser is continuously fired to create a series of lines of treatment. For example, using the diode laser bar 330 of Figure 12B, 12 lines of treatment would appear on the skin (one line for each emitter).

In another embodiment, an optical fiber can couple to the output of each emitter of the diode laser bar. In such an embodiment, the diode laser bar need not be as close to the skin during use. The optical fibers can, instead, couple the light from the emitters to the plate that will be in close proximity to the skin when in use.

Figure 12C shows another embodiment of the invention, which uses multiple diode laser bars to create a matrix of islets of treatment. As shown in Fig. 12C, multiple

diode laser bars can be arranged to form a stack of bars 325. In Figure 12C, for example, the stack of bars 325 includes five diode laser bars. In a similar manner as set forth above in connection with Figure 12A, the stack of bars 325 can be mounted in the housing 313 of a hand piece H101 with the emitters very close to a cooling plate 317.

In operation, the hand piece 310 of Figure 12C can be brought close to the skin surface 319, such that the cooling plate 317 is in contact with the skin. The user can simply move the hand piece over the skin as the diode lasers are pulsed to create a matrix of islets of treatment in the skin. The emission wavelengths of the stacked bars need not be identical. In some embodiments, it may be advantageous to mix different wavelength bars in the same stack to achieve the desired treatment results. By selecting bars that emit at different wavelengths, the depth of penetration can be varied, and therefore the islets of treatment spot depth can also be varied. Thus, the lines or spots of islets of treatment created by the individual bars can be located at different depths.

During operation, the user of the hand piece 310 of Figure 12A or 12C can place the treatment window of the hand piece in contact with a first location on the skin, fire the diode lasers in the first location, and then place the hand piece in contact with a second location on the skin and repeat firing.

In addition to the embodiments set forth above in which the diode laser bar(s) is located close to the skin surface to create islets of treatment, a variety of optical systems can be used to couple light from the diode laser bar to the skin. For example, with reference to Figures 12A and 12C, imaging optics can be used to re-image the emitters onto the skin surface, which allows space to be incorporated between the diode laser bar 315 (or the stack of bars 325) and the cooling plate 317. In another embodiment, a diffractive optic can be located between the diode laser bar 315 and the output window (*i.e.*, the cooling plate 317) to create an arbitrary matrix of treatment spots. Numerous exemplary types of imaging optics and/or diffractive optics that can also be used in this embodiment of the invention are set forth in the section entitled Devices and Systems for Creation of Islets (Example 2) above.

Another embodiment of the invention is depicted in Figure 12D. In this embodiment, the housing 313 of the hand piece 310 includes a stack 325 of diode laser

bars and a plate 317 as in previous embodiments. This embodiment, however, also includes four diffractive optical elements 330 disposed between the stack 250 and the plate 317. In other embodiments, more or fewer than four diffractive optical elements 330 can be included. The diffractive optical elements 330 can diffract and/or focus the energy from the stack 325 to form a pattern of islets of treatment in the skin 319. In one aspect of the invention, one or more motors 334 is included in the hand piece 310 in order to move the diffractive optical elements 330. The motor 334 can be any suitable motor, including, for example, a linear motor or a piezoelectric motor. In one embodiment, the motor 334 can move one or more of the diffractive optical elements 330 in a horizontal direction so that those elements 330 are no longer in the optical path, leaving only one (or perhaps more) of the diffractive optical elements 334 in the optical path. In another embodiment, the motor 334 can move one or more of the diffractive optical elements 330 in a vertical direction in order to change the focusing of the beams.

In operation, by incorporating more than one diffractive optics 330 in the hand piece 310 along with a motor 334 for moving the different diffractive optics 330 between the stack 325 of diode laser bars and the plate 317, the diffractive optics 330 can be moved in position between the stack 325 and the cooling plate 317 in order to focus the energy into different patterns. Thus, in such an embodiment, the user is able to choose from a number of different islets of treatment patterns in the skin through the use of the same hand piece 310. In order to use this embodiment of the invention, the user can manually place the hand piece 310 on the target area of the skin prior to firing, similar to the embodiments described earlier. In other embodiments, the hand piece aperture need not touch the skin. In such an embodiment, the hand piece may include a stand off mechanism (not shown) for establishing a predetermined distance between the hand piece aperture and the skin surface.

Figure 12E shows another embodiment of the invention. In this embodiment, optical fibers 340 are used to couple light to the output/aperture of the hand piece 310. Therefore, the diode laser bar (or diode laser bar stacks or other light source) can be located in a base unit or in the hand piece 310 itself. In either case, the optical fibers couple the light to the output/aperture of the hand piece 310.

In the embodiment of Figure 12E, the optical fibers 340 may be bonded to the treatment window or cooling plate 317 in a matrix arrangement with arbitrary or regular spacing between each of the optical fibers 340. Figure 12E depicts five such optical fibers 340, although fewer or, more likely, more optical fibers 340 can be used in other embodiments. For example, a matrix arrangement of 30 by 10 optical fibers could be used in one exemplary embodiment. In the depicted embodiment, the diode laser bar (or diode laser bar stacks) is located in the base unit (which is not shown). The diode laser bar (or diode laser bar stacks) can also be kept in the hand piece. The use of optical fibers 340 allow the bar(s) to be located at an arbitrary position within the hand piece 310 or, alternatively, outside the hand piece 310.

As an example of an application of a diode laser bar to create thermal damage zones in the epidermis of human skin, a diode laser bar assembly, as depicted in Figures 17 and 18, emitting at a wavelength  $\lambda=1.47\text{ }\mu\text{m}$ , was constructed and applied to human skin ex vivo at room temperature in a stamping mode (that is, in a mode where the assembly does not move across the skin during use). The diode bar assembly had a sapphire window, which was placed in contact with the skin and the laser was pulsed for about 10 ms. The treated skin was then sliced through the center of the laser-treated zones to reveal a cross-section of the stratum corneum, epidermis and dermis. The resulting thermal damage channels were approximately 100  $\mu\text{m}$  in diameter and 125-150  $\mu\text{m}$  in depth for the 10 mJ per channel treatments.

#### B. Hand piece with speed sensor

According to one embodiment of the invention, an apparatus can include a light emitting assembly for applying optical energy to the target area of the patient's skin, a sensor for determining the speed of movement of the head portion across the target area of the patient's skin, and circuitry in communication with the sensor for controlling the optical energy in order to create islets of treatment. The circuitry can control, for example, pulsing of the optical energy source based on the speed of movement of the head portion across the skin in order to create islets of treatment. In another embodiment, the circuitry can control movement of the energy source within the apparatus based on

the speed of movement of the head portion across the skin in order to treat certain areas of the skin, while not exposing other areas, in order to create islets of treatment..

Figure 15 is a bottom view of an embodiment of the invention that includes a speed sensor for measuring the speed of movement of the hand piece across the patient's skin. The embodiment of Figure 15 can be used, for example, in the embodiment of Figure 12A. That is, the hand piece 310 of Figure 12A can include a housing 310, a diode laser bar 315 (or more than one diode laser bars as in Figure 12C), and a plate 317. Figure 15 shows a bottom view of a hand piece in which it is equipped with a speed sensor 350, 352.

A number of types of speed sensors can be used to measure the hand piece speed relative to the skin surface. For example, the speed sensor can be an optical mouse, a laser mouse, a wheel/optical encoder, or a capacitive imaging array combined with a flow algorithm similar to the one used in an optical mouse. A capacitive imaging array can be used to measure both hand piece speed and to create an image of the treated area. Capacitive imaging arrays are typically used for thumbprint authentication for security purposes. However, a capacitive imaging array can also be used to measure the hand piece speed across the skin surface. By acquiring capacitive images of the skin surface at a relatively high frame rate (for example, 100-2000 frames per second), a flow algorithm can be used to track the motion of certain features within the image and calculate speed.

In the embodiment of Figure 15, two capacitive imaging arrays 350, 352 are located on the bottom of the hand piece, with one on each side of the treatment window 354. The diode laser bar 356 output is directed through the treatment window, that is, through a cooling plate or the like. The orientation of the capacitive imaging arrays 350, 352 can vary in different embodiments of the invention. As the device is moved, both capacitive imaging arrays 350, 352 measure the speed of the hand piece across the patient's skin. The configuration can include circuitry that is in communication with the capacitive imaging arrays 350, 352 to measure the speed and determine an appropriate rate for firing the light source (*e.g.*, diode laser) based on that speed. The circuitry, therefore, can also be in communication with the laser in order to pulse the laser at an appropriate speed. The speed sensor incorporated in the hand piece, therefore, can provide feedback to the laser pulse generator. In some embodiments, after an initial pulse

of radiation, the pulsing of the diode laser bar 356 might not be enabled until the capacitive imaging arrays 350, 352 sense movement of the hand piece over the skin. This circuitry can be located in the hand piece in some embodiments or, in other embodiments, in a base unit. When the diode laser bar 356 is enabled for firing by the user (for example by depressing a footswitch), a laser pulse generator for the laser fires the laser at a rate proportional to the hand piece speed.

In operation, the embodiment described above can be used to create a uniform matrix of treatment islets by manually moving a hand piece that includes a single diode laser bar (or multiple diode laser bars) across the skin surface and pulsing the laser at a rate proportional to the hand piece speed. For example, decreasing the time interval between laser pulses as the hand piece speed increases can be used to keep a constant matrix of lines of islets of treatment on the skin. Similarly, increasing the time interval between laser pulses as the hand piece speed decreases can be used to keep a constant matrix of lines of islets of treatment on the skin. The treatment head, including treatment window or light aperture of the hand piece, can be rotated to vary the spacing between islets of treatment in the direction orthogonal to hand piece movement.

In addition to measuring hand piece speed, the capacitive imaging arrays 350, 352 can also image the skin after the line of islets of treatment has been created in order to view the treatment results. Acquired images can be viewed in real time during treatment. The hand piece can include, for example, a display that shows the treatment area of the skin under the cooling plate. Alternatively, the acquired images can be stored in a computer for viewing after the treatment is complete. In some embodiments, the system can be configured to display images from both sensors, so that the hand piece can be moved either forward or backward.

In the configurations discussed above, the diode laser is used at a relatively low duty cycle because the laser is turned off in between islets of treatment. In some embodiments of the invention, the diode laser can be used more efficiently by keeping the diode laser on for a longer time, for example, if the of islets of treatment are lines instead of spots. Figure 16 depicts an example of a hand piece 310 in which the diode laser bar 315 can be mounted on a miniature linear translator 372 inside the hand piece. The hand piece 310 of Figure 16 can be largely the same as the embodiments set forth

above. That is, it can include a diode laser bar 315 adjacent a plate 317 in a hand piece. This embodiment, however, also include a miniature linear translator 372 that can move the diode laser bar 315 in the forward or backward direction within the hand piece 310. Other suitable motors, such as, for example, a piezoelectric motor or any type of linear motor, can be used instead of the miniature linear translator 372. In alternative embodiments, the diode laser bar 315 can be mounted on a cylindrical shaft that can be rotated to accomplish the same function as the linear translator 372. A single-axis galvanometer-driven mirror can also be used.

In the embodiment of Figure 16, as the hand piece 310 is moved forward (left in the Figure), the diode laser bar 315 would be moved backward (right in the Figure) within the hand piece at the same speed. After the diode laser bar 315 reaches the rear of the hand piece 310, it would be moved to the front of the hand piece, and the cycle would be repeated. The spacing between the lines of islets of treatment can be adjusted by varying the time required to move from the rear to the front of the hand piece 310. In this embodiment, for example, a speed sensor can measure the speed of movement of the hand piece 310 across the skin. This speed sensor can be similar to those described above. Such a speed sensor can be in communication with circuitry that moves the diode laser bar 315 (through the motor 372) based on the speed of the hand piece 310 across the skin. Thus, by appropriately moving the diode laser bar 315 within the hand piece 310, a matrix of treatment islets can be created on the patient's skin.

Figures 41A and 41B illustrate another embodiment of the invention that includes a speed sensor. In this embodiment, the hand piece 400 includes a non-coherent EMR source 404 disposed within the housing 402 of the hand piece 400. The non-coherent EMR source 404 can be any of the types set forth above, including, for example, a linear flash lamp, an arc lamp, an incandescence lamp, or a halogen lamp. In one embodiment, the light source 404 is a Xe-filled linear flash lamp.

The hand piece 400 can also include an optical reflector 406, one or more optical filters 408, and a light duct 410 (or concentrator). The optical reflector 530 can serve to reflect and direct the light into the concentrator 410. The concentrator 410 can be made from glass BK7, and can have a trapezoidal shape. In other embodiments, the concentrator 410 can be made from different materials and its shape can vary. The

concentrator 410 can be used, for example, for homogenization of the beam. In some embodiments, the optical filter 408 might not be used. If used, the filter 408 can serve to filter out certain wavelengths of light from the EMR source 404. In addition, the optical reflector 406 might not be used in some embodiments. In some embodiments, a cooling plate (not shown in Figures 41A and 41B) can be attached to the housing 402 or at the end of the optical path in order to cool the patient's skin.

The housing 402 can be equipped with a speed sensor 412. This speed sensor 412 can measure the speed of movement of the housing 402 with respect to the patient's skin. In the embodiment of Figures 41A and 41B, the housing 402 of the hand piece 400 is capable of movement independently from the light source 404 within the housing 402. That is, when the housing 402 moves with a speed  $V$  with respect to the patient's skin, the light source 404 can move within the housing 402 such that the light source 404 remains fixed with respect to the patient's skin. That is, the speed  $v$  of the light source 404 with respect to the patient's skin is approximately zero, which means that the light source 404 would move relative to the housing and within the housing at a speed of  $-V$ . In this embodiment, the light source 404 does not move and is held steady during application of radiation in order to guarantee the desired energy exposure. When treatment of the selected part of skin has been completed, the light source 404 can move within the housing 402 in order to reach its initial position. That is, the light source 404 can move forward in a leap-frog manner with a speed  $v > V$  (where both  $v$  and  $V$  are measured relative to the patient's skin) for treatment of the next part of skin. Such a leap-frog motion is set forth in Figure 41B.

As set forth above, for synchronization of the speed  $V$  of the housing 402 and the speed  $v$  of the light source 404, the housing 402 is equipped with the speed sensor 412. The speed sensor 412 can measure the movement of the housing 402 with respect to the patient's skin and then move the light source 404 within the housing 402 at an appropriate speed in order to remain fixed with respect to the patient's skin. The hand piece 400 or a base unit associated with the hand piece 400 can include circuitry that receives the speed of movement of the housing 402 and then sends a signal to a motor that moves the light source 404 within the housing 402 at an appropriate speed. The hand



piece 400, therefore, can include a linear motor or linear translator, such as those set forth above, to move the light source 404 within the housing 402.

The description above indicates that the light source 404 is moveable within the housing 402. The reflector 406, the filter 408, and the concentrator 412, if used, can be connected to the light source 404 in some embodiments in a manner so that these components move within the housing 402 along with the light source 404. Figure 41B depicts an embodiment in which these components move along with the light source 404.

In some embodiments using a Xe-filled linear flash lamp, the spectral range of the EMR is 300 – 3000 nm, the energy exposure up to  $1000 \text{ J/cm}^2$ , the pulse duration is from about 0.1ms to 10s, and the fill factor is about 1% to 90 %.

Another embodiment of the invention involves the use of imaging optics to image the patient's skin and use that information to determine medication application rates, application of EMR, or the like in order to optimize performance. For instance, some medical or cosmetic skin treatments require that the medication application rate be accurately measured and its effect be analyzed in real time. The skin surface imaging system can detect the size of reversible or irreversible holes created with techniques proposed in this specification for creating treatment islets in the stratum corneum. For this purpose, a capacitive imaging array can be used in combination with an image enhancing lotion and a specially optimized navigation / image processing algorithm to measure and control the application rate.

The use of a capacitive imaging array is set forth above in connection with Figure 15. Such capacitive image arrays can be used, for example, within the applicator 282 of Figure 40 according to this embodiment of the invention. As set forth above, in addition to measuring hand piece speed, the capacitive imaging arrays 350, 352 (Figure 15) can also image the skin. Acquired images can be viewed in real time during treatment via a display window of the device.

One example of a suitable capacitive sensor for this embodiment of the invention is a sensor having an array of 8 image-sensing rows by 212 image-sensing columns. Due to inherent limitations of capacitive array technology, a typical capacitive array sensor is capable of processing about 2000 images per second. To allow for processing skin images in real time, an orientation of the sensor can be selected to aid in functionality. In

one embodiment, for instance, the images are acquired and processed along the columns. This allows for accurate measurement of velocity up to about 200 mm/s.

For the sensor to function reliably and accurately, the skin surface can be treated with an appropriate lotion. The selection of the lotion can be important to the light-based skin treatment and navigation sensor operation. The lotion should be optically transparent to the selected wavelength, provide image enhancement to a sensor, and function as a friction reduction lubricant.

Circuitry containing a processing algorithm or the like can be in communication with the capacitive image sensor. The capacitive sensor and its associated processing algorithm are capable of determining a type of lotion and its effect on the skin surface. This can be performed in real time by sequentially analyzing the image spectral characteristics. The processing algorithm can also perform sensor calibration, image contrast enhancement, and filtering, as well as processing and control of images of the skin surface with navigation code to aid in various applications.

Real time acquired images can be used for statistical analysis of a marker concentration in a lotion. The markers are put in a lotion to function as identifiers of a treatment area. The marker can be a chromophore itself (*i.e.*, a chromophore that heats up upon application of irradiation) or it can be a chemical that indicates the presence of the chromophore or medication in the lotion. As one example, the marker emits or reflects light proportional to the incident light to indicate the concentration of a chromophore or medication in the lotion. The capacitive sensor, therefore, can function to determine whether the marker concentration of a given lotion is at an appropriate level. The circuitry can, for instance, send a signal to the user of the concentration of the marker. Alternatively, the circuitry can determine if the marker concentration meets a preselected set point concentration level for a certain marker. If the set point is not met, the circuitry can communicate to the user to let the user know that more (or perhaps less) lotion may be needed on the patient's skin. Selected markers with the right lotion pH level can also be used as an eye safety enhancement feature for light treatment on human body.

The sensor can also function as a contact sensor. This allows for real time determination of immediate contact of a hand piece with the patient's skin. The

combination of hardware and software allows this determination within one image frame. The algorithm measures in real time a skin contact and navigation parameters (position, velocity and acceleration) along the x-axis and y-axis. This enhances the safety of light treatment on human skin by allowing for the control of the velocity and the quality of skin contact. The quality of contact can be a function of lotion type and pressure applied to the treatment device.

The capacitive sensor along with image processing and special lotion can be used for detecting a skin imperfection and measuring its size in real time. The resolution of the sensor will depend on pixel size, image processing and the sub pixel sampling.

The capacitive sensor and image processing allow for determination of whether the device is operating on biological skin or some form of other surface. It is possible under proper sampling conditions to extract the type of skin the device is moving across. This is accomplished by comparing real time processed images to a stored pattern or calculated set of parameters. In addition, the combination of the capacitive sensor and image pattern recognition, navigation algorithm, and special lotion, can be used to determine the presence of skin hair and provide statistical information about the density and size of the hair.

The capacitive sensor with a combination of two types of lotion, a calibrated skin penetration lotion and image enhancing lotion, can determine the effect of skin rejuvenation on skin over a large area. This analysis can be performed in real time by treating the skin with two lotions and then moving the capacitive sensor over the skin area of interest. The real time algorithm determines the effective area of treatment and the enhancement factor above the norm.

### C. Mirror with holes

Figures 7 and 8 illustrate embodiments of the invention in which the islets of treatment are formed generally through the use of a mirror containing holes or other transmissive portions. Light passes through the holes in the mirror and strikes the patient's skin, creating islets of treatment. Light reflected by the mirror stays in the optical system and through a system of reflectors is re-reflected back toward the mirror which again allows light to pass through the holes. In this manner, the use of a mirror

containing holes can be more efficient than the use of a mask with holes, where the mask absorbs rather than reflects light.

In the embodiment of Figure 7, the patterned optical radiation to form the islets of treatment is generated by a specially designed laser system 420 and an output mirror 422. The laser system 420 and output mirror 422 can be contained in, for instance, a hand piece. In other embodiments, the laser system 420 can be contained in a base unit and the light passing through the holes in the mirror can be transported to the hand piece aperture through a coherent fiber optic cable. In still other embodiments, the laser can be mounted in the hand piece and microbeams from the laser can be directed to the skin with an optical system. In the illustrated embodiment, the laser system 420 comprises a pump source 426, which optically or electrically pumps the gain medium 428 or active laser medium. The gain medium 428 is in a laser cavity defined by rear mirror 430 and output mirror 422. Any type of EMR source, including coherent and non-coherent sources, can be used in this embodiment instead of the particular laser system 420 shown in Figure 7.

According to one aspect of the invention, the output mirror 422 includes highly reflective portions 432 that provide feedback (or reflection) into the laser cavity. The output mirror 422 also includes highly transmissive portions 434, which function to produce multiple beams of light that irradiate the surface 438 of the patient's skin 440. Figure 7 depicts the highly transmissive portions 434 as being circular shapes, although other shapes, including, for example, rectangles, lines, or ovals, can also be used. The transmissive portions 434 can, in some embodiments, be holes in the mirror. In other examples, the transmissive portions 434 include partially transparent micro mirrors, uncoated openings, or openings in the mirror 422 with an antireflection coating. In these embodiments, the rest of the output mirror 422 is a solid mirror or an uncoated surface.

In one implementation, the output mirror 422 functions as a diffractive multi-spot sieve mirror. Such an output mirror 422 can also serve as a terminal or contact component of the optical system 420 to the surface 438 of the skin 440. In other embodiments, the output mirror 422 can be made from any reflective material.

Because of the higher refractive index of the illuminated tissue of the skin 440, divergence of the beams is reduced when it is coupled into the skin 440. In other embodiments, one or more optical elements (not shown) can be added to the mirror 422

in order to image a sieve pattern of the output mirror 422 onto the surface of the skin 440. In this latter example, the output mirror 422 is usually held away from the skin surface 438 by a distance dictated by the imaging optical elements.

Proper choice of the laser cavity length  $L$ , operational wavelength  $\lambda$  of the source 426, the gain  $g$  of the laser media 428, dimensions or diameter  $D$  of the transmissive portions 434 (*i.e.*, if circular) in the output mirror 422, and the output coupler (if used) can help to produce output beams 436 with optimal properties for creating islets of treatment. For example, when  $D^2/4\lambda L < 1$ , effective output beam diameter is made considerably smaller than  $D$ , achieving a size close to the system's wavelength  $\lambda$  of operation. This regime can be used to produce any type of treatment islets.

Typically, the operational wavelength ranges from about 0.29  $\mu\text{m}$  to 100  $\mu\text{m}$  and the incident fluence is in the range from 1  $\text{mJ}/\text{cm}^2$  to 100  $\text{J}/\text{cm}^2$ . The effective heating pulse width can be in the range of less than 100 times the thermal relaxation time of a patterned compound (*e.g.*, from 100 fsec to 1 sec).

In other embodiments, the chromophore layer is not used. Instead the wavelength of light is selected to directly create the pathways.

In one example, the spectrum of the light is in the range of or around the absorption peaks for water. These include, for example, 970 nm, 1200 nm, 1470 nm, 1900 nm, 2940 nm, and/or any wavelength  $> 1800$  nm. In other examples, the spectrum is tuned close to the absorption peaks for lipids, such as 0.92  $\mu\text{m}$ , 1.2  $\mu\text{m}$ , 1.7  $\mu\text{m}$ , and/or 2.3  $\mu\text{m}$ , and wavelengths like 3.4  $\mu\text{m}$ , and longer or absorption peaks for proteins, such as keratin, or other endogenous tissue chromophores contained in the SC.

The wavelength can also be selected from the range in which this absorption coefficient is higher than 1  $\text{cm}^{-1}$ , such as higher than about 10  $\text{cm}^{-1}$ . Typically, the wavelength ranges from about 0.29  $\mu\text{m}$  to 100  $\mu\text{m}$  and the incident fluence is in the range from 1  $\text{mJ}/\text{cm}^2$  to 1000  $\text{J}/\text{cm}^2$ . The effective heating pulse width is preferably less than 100 x thermal relaxation time of the targeted chromophores (*e.g.*, from 100 fsec to 1 sec).

The embodiment of Figure 7 can be used to create islets of treatment in the stratum corneum. Controlling permeability of the stratum corneum can also be accomplished by absorption, scattering, or refractive coupling. Skin or topical cooling can be applied to prevent SC damage between the pathways and to control their size.

Figure 8 depicts a second embodiment of a hand piece 450 that uses a mirror in order to reflect portions of EMR, while allowing certain patterns of the EMR to pass through holes in order to create islets of treatment. The embodiment of Figure 8 includes a light source 452 and, in some embodiments, beam-shaping optics 454 and a waveguide 456. These components can be in a hand piece 450, such as those hand pieces set forth above. In other embodiments, the light source 452 can be in a base unit outside of the hand piece 450. The light source 452 can be a laser, a flashlamp, a halogen lamp, an LED, or another coherent or thermal source. In short, the light source 452 can be any type of EMR source as set forth above. The beam-shaping optics 454 can be reflective or refractive and can serve to direct EMR downward toward the output of the hand piece. The beam-shaping optics 454 can generally be disposed above and to the sides of the light source 452. The waveguide 456 can be used, for example, for homogenization of the beam 458.

The hand piece 150 of the embodiment of Figure 8 can also include an output window 460 near the optical output from the hand piece 450. The output window 460 can be coated with a generally non-transparent coating. The coating can be, for instance, a reflective coating, such as a multi-layer dielectric coating. Such a dielectric coating can be selected to have a high reflectance over a spectral band defined by the EMR source 452. If selected to be highly reflective, such a dielectric coating will not absorb a large amount of light causing it to heat up. In addition, the window with the dielectric coating can be cooled if necessary for heat removal from the skin. Such a dielectric coating can be fabricated by vacuum deposition of one or, more likely, multiple dielectric layers. In some embodiments, the output window 460 can be made from a lattice of microlenses that serves to provide spatial modulation of the power density in the lattice of optical islets.

The coating of the output window 460 can have a number of openings (or holes or transmissive portions) 462, which reshape the output beam into a plurality of beamlets 464. The openings 464 can be coated with anti-reflective coatings, or can contain Fresnel or refractive lenses for angular beam shaping. The openings 464 do not necessarily have to be of circular shape, as depicted in Figure 8. The shape of the openings 464 can be

adjusted depending on the skin condition to be treated. For example, the openings 464 can be circular, slits, rectangles, ovals, lines, or irregular shapes. In some embodiments, the shape of the openings 464 can be changed on demand (adaptively) depending on underlying skin conditions by using, for example, an electro-optical or thermo-optical effect.

The device can contain a cooling implement 466 to provide active contact cooling to the treatment area. The cooling implement 466 can be, for example, a sapphire cooling plate that is cooled by a water manifold or the like built into the hand piece, as set forth above. In addition, any other type of cooling implement 466, such as those set forth above, can be used.

The device of the embodiment of Figure 8 can also include a device for monitoring the temperature of the waveguide 456 and/or the patient's skin 470. The temperature monitoring can be done, for example, using an optical device. In such an embodiment, a separate optical source 472 can be used to shine a probing beam 474 onto the output window 460. The reflected light is then detected with a detector 476. When the refractive indices of the layers in the multi-layer dielectric coating (or mirror or output window 460) change as a result of temperature change, the reflection coefficient of the coating changes as well. Thus, a temperature change can be deduced from the reflection measurements. A section 478 of the output window 460 can be optically separated from the skin 470 in order to reduce background parasitic signal from the skin 470 in measuring the temperature of the output window 460. The optical source 472 and the detector 476 can be built into the hand piece.

In some embodiments, the openings 462 in the output window 460 can be coated with phase-changing material, which changes its transparency as a result of temperature change. That is, the transparency of the openings 462 decreases when the temperature increases. Thus, overheating of skin 470 can be prevented by blocking the beamlets 474 with the decreased transparency of the openings 416.

In operation, the output window 460 is brought into contact with the treatment area 470 (*i.e.*, the patient's skin). The light source 452 is then fired to output radiation from the hand piece. The openings 462 in the output window 462 form islets of treatment on the patient's skin 470.

The device of Figure 8 can be used either in the stamping modes or the sliding modes. A stamping mode is a mode in which the device is placed on the skin and the radiation source is activated while the device remains stationary on the skin. In the sliding mode, the device can be moved over the skin while in contact with the skin. In the stamping modes, the resulting temperature in the skin (and, possibly, the damage profile) is completely determined by the geometry of the openings and the illumination/cooling parameters. In the sliding modes, an additional degree of control is available by varying the velocity of scanning.

The device of Figure 8 can have an optical coating (*i.e.*, on the treatment window 460) to provide light spatial modulation. Some embodiments can use technology similar to a gradient mirror, which is a mirror with variable transmission over its radius. An embodiment including a plurality of gradient mirrors could be beneficial for enhancement of parameters of the light source (such as the effect of photon recycling) and system cooling capabilities (very thin coating thickness).

In some embodiment, the coating, (such as, for example, a multilayer dielectric high reflective coating with lattice of transparent zones) can be coated directly on the contact cooling surface of a sapphire chilled block. In such an embodiment, the entire sapphire block can be used as a cooling area, but the irradiated area is limited by the area of the transparent zones. Such an embodiment can be effective for a combination of LOI treatment with skin upper layer protection for deep dermal or fat treatments.

In another embodiment, where a laser source is used, the laser itself can have an output that is not uniform. For example, in such an embodiment, the laser itself can be surrounded by a reflector, which can be a high reflector. The reflector surrounding the laser, and in particular at the output end of the laser, can have areas that are less reflective than other areas. That is, the reflector in such an embodiment does not have uniform reflectivity. These areas can result in increased radiation output from the laser source in discrete areas (or holes). Thus, the reflector or mirror surrounding the laser can itself generate spatially modulated light as an output. The laser source can therefore be housed in a hand piece that has the laser source output close to the output from the hand piece. The hand piece can therefore be brought into close proximity to the skin and fired to create treatment islets.



#### D. Skin lifting implement

Another embodiment of the invention is illustrated in Figure 42A. In this embodiment, a hand piece contains two light-emitting assemblies 520 that are positioned at an angle to each other. Each light-emitting assembly 520 includes a light source 501, a beam-shaping implement 502, and an output window 503. The light source 501 can be any variety of EMR source as set forth above. The beam-shaping implement 502 can be a device to reflect and focus EMR from the light source 501. The output window 503 can be a contact plate for the patient's skin that is similar to those contact or cooling plates set forth above.

The skin-lifting implement 508 is used to create a skin fold of the treatment skin area 505. The skin-lifting implement 508 can be, for example, a vacuum implement. Parameters of the illumination (wavelength spectrum, power, cooling, etc.) can be selected in such a way that beamlets 506 of EMR create an area of sufficient irradiance only in one or more limited spatial zones 507 where the beamlets 506 intersect. Thus, the dimensions of the damage zone (or areas with islets of treatment) can be controlled with high precision. The device of Fig. 42A can contain masks 504 with coatings or reflective surface in the output windows 503 similar to those set forth above in connection with Figures 7 and 8.

In one embodiment, the mask 504 of each assembly 520 can slide with respect to the corresponding window 503. For example, with reference to Figure 42B, the mask 504 is movable within the window 503 so that, for example, the mask stays fixed with respect to the patient's skin for a brief period of time when the hand piece moves over the skin. The mask 504, therefore, can slide within the hand piece at a rate proportional to the speed of movement of the hand piece over the patient's skin in a manner as set forth above. Thus, the mutual positions of the beamlets 506 and, therefore, the zones of overlapping beamlets 506, can be controlled with even greater precision to create islets of treatment in the patient's skin. After a brief period of time in which the mask 504 remains fixed with respect to the patient's skin, the mask 504 leap-frogs in position within the output window 503 in order to treat a different area of the patient's skin.

Like the device of Figure 8, the device of Figure 42A can be used either in the stamping modes or the sliding modes.

Another implementation can be a vacuum chamber surrounding the treatment area. That is, a vacuum change can surround the distal tip of a hand piece (*i.e.*, the portion in contact with the patient's skin). Such an implementation can be beneficial in increasing the density of treatment islets. The vacuum chamber can laterally stretch the skin and keep it stretched and in contact with distal tip during treatment. After releasing of the skin from the vacuum change the skin will reform back to its initial size with significantly denser islets.

The use of such a vacuum changer surrounding the hand piece distal tip can also increase blood circulation, which can benefit treatment of conditions where hemoglobin is a chromophore. A further increase of the vacuum force can bring the skin into direct contact with the tip of the hand piece and in the contact area internal blood pressure will be relived and blood circulation will decrease. If the chamber design allows skin to stretch laterally outside the tip area, further compression of blood vessels will increase skin transparency to certain wavelengths of light and will increase light penetration depth. Another advance of this concept is that a lower temperature and a lower energy level can be used for stretched skin in order to denature the skin. In addition, stretched skin can result in a lower scattering level and better penetration for light.

#### E. Hand pieces with non-coherent light sources to form islets of treatment

Figure 9A shows another embodiment of the invention. In this embodiment, the invention is a hand piece 540 that includes an EMR source 542 and a distal end 544 shaped in a manner to create output light spatial modulation and concentration, and therefore to form islets of treatment in a patient's skin. The EMR source 542 can, in some embodiments, be any of the types of non-coherent sources set forth above, including, for example, a linear flash lamp, an arc lamp, an incandescence lamp, or a halogen lamp. In one embodiment, the light source 542 is a Xe-filled linear flash lamp.

The hand piece 540 can also include an optical reflector 546, one or more optical filters 548, and a light duct 550 (or concentrator). The optical reflector 546 can serve to reflect and direct the light into the concentrator 550. The concentrator 550 can be made from BK7 glass, and can have a trapezoidal shape. In other embodiments, the concentrator 550 can be made from different materials and its shape can vary. The concentrator 550 can be used, for example, for homogenization of the beam. In some

embodiments, the optical filter 548 might not be used. If used, the filter 548 can serve to filter out certain wavelengths of light from the EMR source 542. In addition, the optical reflector 546 might not be used in some embodiments. In some embodiments, a cooling plate (not shown in Figures 9A-E) can be attached to the housing of the hand piece or at the end of the optical path in order to cool the patient's skin.

The distal end 544 of the concentrator 550 can include an array shaped in a manner to create output light spatial modulation and concentration, and therefore to form islets of treatment in a patient's skin. For example, the distal end 544 can include an array of pyramids (Fig. 9B), cones (Fig. 9C), hemispheres (Fig. 9D), grooves (Fig. 9E), prisms, or other structures for output light spatial modulation and concentration. The distal end, therefore, can be made from any type of array, such as micro prisms, that create output modulation and concentration to produce islets of treatment.

In the exemplary embodiment of Figures 9A-E using a Xe-filled linear flash lamp, the spectral range of electromagnetic radiation is about 300 – 3000 nm, the energy exposure is up to about 1000 J/cm<sup>2</sup>, the laser pulse duration is from about 10ps to 10s, and the fill factor is from about 1% to 90%.

Figure 43A shows another embodiment of the invention. In this embodiment, the invention is a hand piece 540 that includes many of the same elements as in the embodiment of Figure 9A. That is, the embodiment of Figure 43A can include an EMR source 542, an optical reflector 546, one or more optical filters 548, a light duct 550 (or concentrator), and a cooling plate (not pictured). Each of these components can be similar to or the same as the components set forth above in connection with Figure 9A.

In the embodiment of Figure 43A, the distal end 544 of the concentrator 550 can be made as an optically diffusive surface with clear (polished) spots for output light spatial modulation. For example, with reference to Figure 43B, which shows a side and a top view of the distal end 544, the distal end 544 can include a scattering film 560 with circular openings 570. The scattering film 560 with circular openings 570 can create output modulation to produce islets of treatment on the patient's skin. In particular, the openings 570 (which can be clear, polished spots) can allow for the passage of EMR in order to create the islets of treatment.

Figure 13A shows another embodiment of the invention. In this embodiment, the invention is a hand piece 540 that includes many of the same elements as in the embodiment of Figures 9A and 43A. That is, the embodiment of Figure 13A can include an EMR source 542, an optical reflector 546, one or more optical filters 548, a light duct 550 (or concentrator), and a cooling plate (not pictured). Each of these components can be similar to or the same as the components set forth above in connection with Figure 9A.

In the embodiment of Figure 13A, the light guide 550 can be made from a bundle of optical fibers 580 doped with ions of rare earth metals. For example, the light guide 550 can be made from a bundle of  $\text{Er}^{3+}$  doped fiber. The active ions inside the light guide core 582 can act as fluorescent (or super fluorescent) converters to provide desired spatial modulation and spectrum conversion. Thus, the light guide 550 in the embodiment of Figure 13A can create spatial modulation of the EMR in order to create islets of treatment.

Figures 13B, 13C, and 13D show embodiments in which the optical fibers 580 are wrapped around the EMR source 542 in order to couple light into the optical fibers 580. As shown in Figure 13C, each individual fiber or group of fibers 580 can have its output directed to the skin. Figure 13D shows a bottom view of the output from the hand piece. As shown in Figure 13D, the fibers 580 can have an output distribution that is spatially modulated in order to create islets of treatment.

Figure 13E shows another embodiment that uses the same general structure as the embodiments of Figures 13A, 13B, and 13C. In the embodiment of Figure 13E, the output of the fiber bundle 580 (*i.e.*, the bundle of Figures 13B-D) can have a distal end that is made from an array of micro lenses 586 attached to the output face of the light guide. The array of micro lenses 586 can serve to focus and concentrate the output from the fiber bundle 580 in order to create islets of damage.

Figure 11 shows another embodiment of the invention. In this embodiment, the invention includes a hand piece 600 with multiple sets of EMR sources 604, reflectors 602, filters 606, and light guides 608. The output of each light guide can also be a cooling plate. Each of these components can be similar to or the same as the components set forth above in connection with Figure 9A. In this embodiment, the spacing between the individual EMR sources (emitters) can provide the desired light spatial modulation in

order to form islets of treatment. Figure 11 shows four sets of EMR sources 604 and associated components. In other embodiments, however, more than or less than four sets of EMR sources 604 can be used. In addition, an array of EMR sources can be used in some embodiments. For instance, such an array could be 4 by 6, for a total array of 24 EMR sources.

#### F. Hand piece with total internal reflection

Figures 10A-10C show another embodiment of the invention in which the output EMR from the hand piece is totally internally reflected when the hand piece is not in contact with a patient's skin. When the hand piece is in contact with a patient's skin, the output EMR is spatially modulated in order to create islets of treatment in the patient's skin.

In the embodiment of Figures 10A-10C, the invention is a hand piece 540 that includes many of the same components as in the embodiment of Figures 9A-E. That is, the embodiment of Figures 10A-10C can include an EMR source 542, an optical reflector 546, one or more optical filters 548, a light duct 550 (or concentrator), and a cooling plate (not pictured). Each of these components can be similar to or the same as the components set forth above in connection with Figure 9A.

The total internal reflection in the embodiment of Figures 10A-10C is caused by the shape of the distal end 544 of the light duct 550. The distal end 550 can be an array of prisms, pyramids, hemispheres, cones, etc..., such as set forth in Figures 10B and 10C. The array of elements have dimensions and shapes that introduce light total internal reflection (TIR) when the distal end 544 is in a contact with air, as shown in Figure 10B. In contrast, the distal end 544 does not cause TIR (it frustrates TIR) when the distal end 544 is in a contact with a lotion or skin surface, as shown in Figure 10C. Further, when the distal end 544 is in a contact with a lotion or skin surface, this leads to light spatial modulation and concentration of the EMR in a contact area of the patient's skin, causing islets of treatment.

In the exemplary embodiment of Figure 10A-10C using a Xe-filled linear flash lamps, the spectral range of electromagnetic radiation is about 300 – 3000 nm, the energy exposure is up to about 1000 J/cm<sup>2</sup>, the laser pulse duration is from about 0.1ms to 10 seconds, and the fill factor is from about 1% to 90%.

The embodiments of Figures 10A, 10B, and 10C depict the use of a non-coherent light source in a hand piece. However, a mechanism can also be used to cause TIR in an embodiment using a coherent light source, such as, for example, a solid state laser or a diode laser bar. Referring to the embodiments of Figures 12A-E, 15 and 16, the light from the diode laser bar 315 (in Fig. 12A) can also be coupled to the skin via a total internal reflection (TIR) prism. Since the diode laser bar 315 might not be located in close proximity to the skin surface, an optical system might be required to re-image the emitters onto the skin. Thus, a distal end with prisms or the like can be used to re-image the emitters onto the skin. In one embodiment, a TIR prism can be used. When the TIR prism is not in contact with patient's skin, light from the diode laser bar would be internally reflected and no light would be emitted from the hand piece. However, when the patient's skin is coated with an index-matching lotion and the skin is brought into contact with the hand piece (and, in particular, the prism), light is coupled into the skin. Thus, in a manner similar to that described above for non-coherent light sources, TIR reflection prisms or arrays can also be used in embodiments using coherent light sources. This feature can be important for eye and skin safety.

#### G. Solid state laser embodiments

Figures 14A, 14B, and 14C show additional embodiments of the invention. Figure 14A shows an embodiment in which the apparatus includes a laser source 620, focusing optics (*e.g.*, a lens) 622, and a fiber bundle 624. The laser source 620 can be any suitable source for this application, for example, a solid state laser, a fiber laser, a diode laser, or a dye laser. In one embodiment, the laser source 620 can be an active rod made from garnet doped with rare earth ions. The laser source 620 can be housed in a hand piece or in a separate base unit.

In the exemplary embodiment as in Figure 14A, the laser source 620 is surrounded by a reflector 626 (which can be a high reflector HR) and an output coupler 628 (OC). In other embodiments, the reflector 626 and the coupler 628 are not used. Various types and geometries of reflectors can be used for reflector 626. The fiber bundle 624 is located optically downstream from the lens 622, so that the optical lens 622 directs and focuses light into the fiber bundle 624.

In one embodiment, an optical element 630, such as a lens array, can be used to direct and output the EMR from the fiber bundle 624 in order to focus the EMR onto the patient's skin 632. The optical element 630 can be any suitable element or an array of elements (such as lenses or micro lenses) for focusing EMR. In the embodiment of Figure 14A, the optical element 630 is a micro lens array. In other embodiments, an optical element 630 might not be used. In such an embodiment, the outputs of the fibers in the fiber bundle 624 can be connected to one side of a treatment window (such as a cooling plate of the apparatus), where the other side of the treatment window is in contact with the patient's skin 632.

In operation, the laser source 620 generates EMR and the reflector 626 reflects some of it back toward the output coupler 628. The EMR then passes through the output coupler 628 to the optical lens 622, which directs and focuses the EMR into the fiber bundle 624. The micro lens array 630 at the end of the fiber bundle 624 focuses the EMR onto the patient's skin 632.

Figure 14B shows another embodiment of the invention. In this embodiment, the apparatus includes a laser source 620 and a phase mask 640. The laser source 620 can be any type of laser source and can be housed in a hand piece or in a separate base unit, such as in the embodiment of Figure 14A. In one embodiment, the laser source 620 can be an active rod made from garnet doped with rare earth ions. Also like the embodiment of Figure 14A, the laser source 620 can be surrounded by a reflector 626 (which can be a high reflector HR) and can output EMR into an output coupler 628 (OC).

The embodiment of the invention of Figure 14B includes a phase mask 640 that is located between the output coupler 628 and an optical element 642. The phase mask 640 can include a set of apertures that spatially modulate the EMR. Various types of phase masks can be used in order to spatially modulate the EMR in order to form islets of treatment on the patient's skin 632. The optical element 642 can be any suitable element or an array of elements (such as lenses or micro lenses) that focuses the EMR radiation onto the patient's skin 632. In embodiment of Figure 14B, the optical element 642 is a lens.

In operation, the laser source 620 generates EMR and the reflector 626 reflects some of it back toward the output coupler 628. The EMR then passes through the output

coupler 628 to the phase mask 640, which spatially modulates the radiation. The optical element 642, which is optically downstream from the phase mask 640 so that it receives output EMR from the phase mask 640, generates an image of the apertures on the patient's skin.

Figure 14C shows another embodiment of the invention. In this embodiment, the apparatus includes multiple laser sources 650 and optics to focus the EMR onto the patient's skin 632. The multiple laser sources 650 can be any suitable sources for this application, for example, diode lasers or fiber lasers. For example, the laser sources 650 can be a bundle of active rods made from garnet doped with rare earth ions. The laser sources 650 can optionally be surrounded by a reflector and/or an output coupler, similar to the embodiments of Figures 14A and 14B.

In the embodiment of Figure 14C, an optical element 642 can be used for focusing the EMR onto the patient's skin 632. Any suitable element or an array of elements (such as lenses or micro lenses) can be used for the optical element 642. The optical element, for example, can be a lens 642.

In operation, the bundle of lasers 650 generate EMR. The EMR is spatially modulated by spacing apart the laser sources 650 as shown in Figure 14C. The EMR that is output from the laser sources 650, therefore, is spatially modulated. This EMR passes through the output coupler 628 to the optical element 642, which focuses the EMR onto the patient's skin 632 to form islets of treatment.

In the exemplary embodiment of Figures 14A, 14B, and 14C, which each use a garnet laser rod doped with rare earth ions, the spectral range of electromagnetic radiation is about 400 – 3000 nm, the energy exposure is up to about 1000 J/cm<sup>2</sup>, the laser pulse duration is from about 10ps to 10s, and the fill factor is from about 1% to 90%.

#### H. Consumer-Oriented Products and Methods

In another aspect, the invention can involve creating many zones of increased permeability in the SC without causing irreversible structural damage, or minimizing such damage, to the tissue. Reversible permeability is achieved by creating permeability of a topical in the SC for a limited time. Generally, this limited time corresponds to the application of EMR energy. After application of the EMR energy, the SC closes. Alternatively, permeability may remain for a period of time after application of the EMR



energy. The time for permeability should be achieved in a limited time to prevent risk of infection. Using the principles of the present invention, such treatment can be made safe and painless, and thus can be practiced, for example, by members of general public, *i.e.*, individuals with no special training. One such use is for enhancing the delivery of topical cosmetic compositions or pharmaceutical agents during in-home application.

Figure 44 is a schematic of a hand piece 670 according to this embodiment of the invention. In one example, the hand piece 670 emits a pattern 672 of beamlets 674 that irradiate the surface 676 of the skin 680. It creates thermal zones, *e.g.*, moderate hyperthermia, in the skin to thereby create temporary permeability paths 682. The temporary permeability paths 682 can be created by inducing a series of phase transitions in the intercellular lipids connecting corneocytes of the stratum corneum layer 684. Lipids in the SC start to melt at about 35 C and completely melt at about 85 C. The hand piece 670 can also include a vibrator for skin massaging and/or an ultrasound or iontophoresis enhancer of permeability.

The hand piece 670 in one example uses an internal array of waveguides or an array of light emitting diodes (LED) or laser diodes to create the beamlet pattern 672. Suitable examples of LEDs or laser diodes are set forth above in connection with other embodiments. For example, a one-dimensional array of diode lasers or a stack of light emitting diode bars can be used. Numerous other types of EMR sources can also be used in this embodiment. In some embodiments, hand piece 670 can include multiple light sources for topical photo activation inside skin. In some embodiments, the wavelength of light is selected so that the skin is not damaged, but the SC become permeable for a limited period of time.

For controlled heating of the SC, endogenous or exogenous chromophores can be used. For endogenous chromophores, water, lipids or proteins can be used. In one example, the spectrum of the light is in the range of or around the absorption peaks for water. These include, for example, 970 nm, 1200 nm, 1470 nm, 1900 nm, 2940 nm, and/or any wavelength > 1800 nm. In other examples, the spectrum is tuned close to the absorption peaks for lipids, such as 0.92  $\mu\text{m}$ , 1.2  $\mu\text{m}$ , 1.7  $\mu\text{m}$ , and/or 2.3  $\mu\text{m}$ , and wavelengths like 3.4  $\mu\text{m}$ , and longer for absorption peaks for proteins, such as keratin, or other endogenous tissue chromophores contained in the SC.

As a result of the phase transitions, balance between solid and liquid phases of lipids shifts towards the latter. This, in turn, leads to the development of enhanced permeability paths (not pictured) through the SC. Molecules, molecular complexes, or particles of a topical composition 694 may be discharged from (or through) an applicator 688 of the hand piece 670 or applied directly to the skin and penetrate through the paths 682 into the epidermis and dermis due to enhanced diffusion. The topical composition can be applied to the skin before, during, or after EMR treatment corresponding to the time that the SC has enhanced permeability.

In some embodiments, the bottom plate 690 of the hand piece 670 is cooled to increase skin safety and comfort as well as to accelerate restoration of the normal permeability of the SC after having delivered the composition. In other embodiments, the plate 690 is heated to facilitate the process of the pathway creation. Additional topical compound can be used after treatment to accelerate healing of SC after treatment.

In some embodiments, the thermal regimen can be reversed. For example, the hand piece 670 can create zones of hypothermia at the skin surface 676 in order to initiate the process of "freezing" of lipids in the SC. As a result, the lipid component shrinks and paths of facilitated percolation can be created. The formula above still holds, with minimal allowable temperature at the basal membrane approximately 15-18 C. The plate in such an embodiment can be heated for better skin protection and speedy restoration of the permeability.

This concept can be used for temporal delivery of cosmetic compounds into the skin, preferable into the epidermis. The compound can be removed from the skin with the growth of the epidermis. In addition, the compound can be used for skin whitening or darkening, better scattering, and tattooing.

### EXAMPLE 5

#### Thermal Permeation of the Stratum Corneum

Lattices of thermal islets can be used to increase the permeability of the stratum corneum layer in a variety of ways, and to varying degrees, in accordance with the invention.

At temperatures in the range of 35-40°C, the outer most layers of the skin are subject to "soft hyperthermia" which is sufficient to increase the diffusion of some compounds into and through the stratum corneum and stratum lucidum. The permeability increases with "moderate hyperthermia" at temperatures in the range of 40-50°C. These temperatures are sufficient to initiate a phase change which partially melts or liquefies the typically crystalline lipid intercellular matrix of the stratum corneum and stratum lucidum. Generally, changes induced by this moderate heating, however, are reversible. After the heat source is removed, the lipid intercellular matrix recrystallizes with little or no permanent change. At temperature in the range of 50-100°C, the skin is subjected to "strong hyperthermia" which causes modification of the structure of the stratum corneum and stratum lucidum that is only partially reversible. By 85°C, lipid intercellular matrix is completely liquefied. Heating the stratum corneum to temperatures of 100-200°C causes evaporation of water and induces irreversible disruption of the stratum corneum to form micro gaps, but does not remove the stratum corneum. Rapid heating of the stratum corneum to temperatures greater than 200°C causes denaturation of the proteins of horny cells and vaporization of the lipids or water of the stratum corneum structure. The resulting pressure waves from the vaporization can create holes in the stratum corneum.

Moderate and strong hyperthermia typically induce a pain response in a subject. Generally, the sensory nerves in the papillary dermis serve to sense and transmit heat, pain, and other noxious sensations. When exposed to temperatures in excess of 40-43°C, these sensory nerves will transmit a pain response in most subjects. Thus, moderate and strong hyperthermia typically require at least local anesthesia if applied uniformly or continuously on the skin surface. The local anesthesia can be achieved, for example, either by using topical formulations (*e.g.*, lidocaine, LMX4™, Ferndale Laboratories, Inc., Ferndale, MI) or by pre-cooling the treatment area in order to decrease the sensitivity of the skin.

#### 1. EMR-absorbing Particles

In some embodiments, the invention provides a film with a lattice of EMR-absorbing particles in the form of dots, lines or other shapes, either on the surface of the film or embedded within the film. The EMR-absorbing particle arrangement can be

random, or can have a regular pattern, such as a grid structure. For example, the material of the film can be a transparent, temperature-stable, preferably flexible composition with low thermal conductivity, such as an optically clear polymer; whereas the material of the EMR-absorbing particles is a substance, such as carbon, ink, or metal, which is appropriate to the EMR source. The EMR-absorbing particles can be spheres with diameters of 1-1000  $\mu\text{m}$ , typically 50-500  $\mu\text{m}$ . The spheres can be packed into the film with a fill factor of about 1-100 %. For higher fill factors, such as about 50-100%, the film plays the additional role of protecting the skin from light. The size of a resulting thermal islet on the skin can be smaller or larger than an EMR-absorbing particle depending on particle temperature, degree of contact of the particle with the skin, and the presence of other substances (*e.g.*, oil, lotion, vaseline) with appropriate thermal properties at the particle/skin interface that may help to conduct heat away or keep the heat of the particle confined to the particle/skin interface.

In some embodiments, the film can include additional waveguides on top of the EMR-absorbing particles. In certain embodiments, the waveguides can be cone-shaped. The purpose of the waveguides is to provide additional concentration of EMR energy into the islets. This can be achieved, for example, by using a transparent material with a refractive index higher than that of the film, and utilizing the phenomenon of the total internal reflection (TIR).

In another aspect of the invention, the film or the EMR-absorbing particles of the film can be impregnated with a cosmetic or therapeutic agent to be delivered through the stratum corneum. In these embodiments, the EMR-absorbing particles contain cavities which are filled with the agent intended for delivery, and have openings oriented towards the skin surface. Initially, the openings are closed by plugs to prevent leakage of the agent. When EMR energy is applied, the EMR-absorbing particles are heated and produce thermal islets with increased permeability in the skin. The material of the plugs is selected such that it is melted by the temperature increase, allowing the release of the agent to the thermal islets. In addition, in some embodiments, the contents of the particles can expand and form a series of jet-like streams directed toward the skin.

In one specific embodiment, a film with a pattern of carbon dots is employed. The carbon dots can be embedded in the film, or can be transferred from the film onto the

skin and the film removed. For example, the carbon dots can be transferred by a first laser pulse, and then the dots on the skin can be irradiated by a second laser pulse or by irradiation from another source.

In some embodiments, the plurality of EMR-absorbing particles is exposed to EMR in the form of a uniform incident optical beam. Such a beam can be generated by, for example, a laser or flash lamp. The exposed particles absorb the radiation and release it as heat into the underlying areas of the stratum corneum, increasing the permeability of the stratum corneum and creating enhanced permeability paths for delivery of the agent.

The wavelength(s) of EMR used for exposure of the EMR-absorbing particles can be important. For example, the wavelength(s) can be in the range of approximately 290 nm to approximately 1000  $\mu\text{m}$ . Generally, the wavelength(s) can be poorly absorbed in the body, particularly the skin, but well absorbed by the EMR-absorbing particles. The ratio of the absorption coefficient of the EMR-absorbing particles to the absorption coefficient of skin should be greater than 1. Thus, when irradiated, the EMR-absorbing particles will be preferentially heated and will transfer heat to the stratum corneum layer of the underlying skin. In contrast, EMR that does not strike the particles will not be absorbed efficiently by the skin and, in addition, the resulting heat will be distributed over a large depth profile within the skin, resulting in only diffuse heating, avoiding significant local heating and damage to the skin or other structures.

In some embodiments, the incident fluence is in the range of 1  $\text{mJ}/\text{cm}^2$  to 1000  $\text{J}/\text{cm}^2$ . If highly absorbing particles are used, typically 1  $\text{mJ}/\text{cm}^2$  is required per 20°C of heating of the stratum corneum.

In some embodiments, the incident radiation can be applied in a pulsed fashion to minimize damage to the epidermis and dermis. The effective heating pulse width should be less than 100 times the thermal relaxation time of the islets. Thus, pulse widths are typically in the range of 100 femto seconds to 1 second, depending on the islet size that is selected.

In addition to the use of films, as set forth above, the invention can be practiced by providing a topical composition that includes EMR-absorbing particles (*e.g.*, chromophores) in a liquid carrier, such as a solution, suspension, cream or lotion. The topical composition can be applied to the skin, resulting in a random distribution of the

EMR-absorbing particles on the surface. The density of the EMR-absorbing particles on the surface can be controlled by varying the concentration of the EMR-absorbing particles in the topical composition, or by varying the amount of the topical composition which is applied. Upon application of the EMR source, the EMR-absorbing particles can warm up, thus selectively producing thermal islets of treatment. Any of the variety of materials set forth above for EMR-absorbing particles can be used in the topical composition.

In another embodiment, a spatially selective pattern of EMR-treated islets can be created by applying to the skin surface a desired pattern of a topical composition containing a preferentially absorbing exogenous chromophore. First, a desired pattern of the composition is applied to the selected skin treatment area using a printing head mounted on a scanner. Next, an EMR delivery system delivers a beam of radiation to the treatment area, thus preferentially heating the composition. The resulting heat diffusion from the patterned chromophores of the composition yields a corresponding pattern of thermal islets. The dimensions of a thermal islet can, for example, vary between 1  $\mu\text{m}$  and 3 mm, and the distance between the islets can, for example, vary between 1 and 1000 times their dimensions.

In another embodiment, instead of applying the topical composition directly to the skin surface, the composition can be applied first to an EMR-transparent film. Then, the film can be applied to the skin surface, and the radiation can be delivered through the film. The spectral composition of the incident radiation should match the absorption spectrum of the chromophore. Any of a variety of substances can be used as chromophores in this embodiment including, but not limited to, carbon, metals (*e.g.*, Au, Ag, Fe), organic dyes (*e.g.*, methylene blue, toluidine blue, trypan blue), non-organic pigments, and fullerenes. Fluences of the radiation can, for example, range from 0.1 to 1000 J/cm<sup>2</sup>, and pulse width can, for example, range from 1 ps to 10 sec. The desired pattern need not be regular or pre-determined. It can vary as a function of the skin condition at the desired treatment area or be generated *ad hoc* by the physician or technician.

In another embodiment, all of the features described with respect to a film can be implemented at the distal end of a light source which is contacted to the skin.

In another embodiment, the hand piece of an EMR source can be scanned along the skin surface. A tracking/imaging device (*e.g.*, digital camera or capacitance array) in the hand piece can detect, segment, and follow target volumes (*e.g.*, pigmented lesions or vascular abnormalities). An EMR-absorbing particle (*e.g.*, chromophore) dispenser in the hand piece can dispense the EMR-absorbing particles according to the tracking information, following projection of the target on the skin surface. The EMR source can then irradiate the EMR-absorbing particles dispensed in the treatment area.

Another embodiment is a dermatological delivery device that includes a substrate. According to this embodiment, the substrate has a plurality of absorbing elements, such as those set forth above, and a composition contained on at least one side of the substrate. Incident radiation from an energy source can heat up the absorbing elements so that the absorbing elements create treatment islets in the stratum corneum of a person's skin. After removal of the substrate, at least a substantial portion of the composition remains on the person's skin. That is, the composition, which can be cosmetic, therapeutic, or medical, can be attached to or disposed within or on the substrate in a manner so that at least some meaningful portion of the composition remains on the skin when the substrate is removed.

When the goal of treatment is to facilitate penetration of a cosmetic or therapeutic agent, the tracking/imaging device can be replaced with a dispenser for the agent.

## 2. Exothermic Compounds

In other embodiments, a film is employed which includes particles of an exothermic compound, and the particles are held in close proximity to or deposited onto the skin surface.

In some embodiments, small volumes of the exothermic compound 780 are attached to or embedded in a film 782 or other carrier, as shown in Figure 47. Application of this film 782 to the surface of the skin 784 holds the compound in a heat conductive relationship with the skin 784. In certain embodiments, light or electrical discharge (as shown originating from light source 788) is used to ignite (initiate) a reaction of the exothermic compound, which leads to a controlled release of the chemical energy into the underlying stratum corneum. For example, a mixture of a light-absorbing chromophore (*e.g.*, carbon) with an exothermic reagent (*e.g.*, nitroglycerin) can be used.

The chromophore absorbs the energy, and releases it as heat that ignites the exothermic reagent.

### 3. Patterned Radiation

In other embodiments, a continuous or mostly continuous coating of an EMR-absorbing compound is applied to the skin. For example, carbon paper, dye solution, or a thin layer of an EMR-absorbing lotion can be used. The EMR source must have a spectrum that matches the absorption peaks of the EMR-absorbing compound. For example, if water is used as the EMR-absorbing compound, the spectrum can include wavelengths of approximately 1.45, 1.9 and  $> 2.3 \mu\text{m}$ .

The continuous coating is then exposed to a pattern of EMR. The EMR pattern can be produced using a source of uniform radiation, such as a laser or flash lamp, and an amplitude or phase mask or other delivery system for producing optical islets or beamlets of the pattern. Alternatively, the beamlets can be produced through multiple sources, such as multiple diode laser emitters or fiber bundles, for example. The beamlets locally heat the EMR-absorbing compound (*e.g.*, chromophore) coating, which then creates thermal islets.

In another example, an interference pattern (*e.g.*, Moire pattern) is created by a source at the skin surface. The patterns are designed such that the intensity at the nodes, or regions of constructive interference, exceeds a threshold for creating the permeability paths through the stratum corneum whereas the intensity between the nodes remains below the threshold.

In a particular embodiment, the patterned radiation can be a periodic lattice. The parameters of the patterned radiation are controlled by selecting the geometry of the incident beam, source settings, and properties of the EMR-absorbing compound, as well as its concentration.

### EXAMPLE 6

#### Rapid Acne Treatment Device

Another embodiment of the invention is shown in Figures 49A-B, 50, and 51A-B. The purpose of the device of this embodiment is rapid reduction of volume and redness of inflammatory acne lesions (single lesion treatment). For example, the reduction in



redness and inflammation may occur within about 8-12 hrs. Although these embodiments are described for use in acne treatment, there are other possible uses of these embodiments as well.

#### A. Acne treatment device with bulk output

Figures 49A, 49B, and 50 show one embodiment of the acne treatment device. In this embodiment, the primary role of the light 842 is to facilitate delivery of a topical medication through the stratum corneum without seriously compromising the skin barrier function. Optionally, the light can also provide an additional benefit in mitigating the acne, independent of the topical medication. The system in this embodiment includes an applicator 840 to deliver light and a patch 844, which can contain a topical medication and which can also heat upon exposure to light, facilitating penetration of the stratum corneum. This medication can be result in vascular contraction, an anti-inflammatory effect, and reduction of bacterial. It can also be medication with a PDT effect.

In this embodiment, the device is a pulsed-light system, implemented as a hand-held cordless applicator 840 and a charger 850. In this embodiment, the applicator 840 can be a stand-alone device. In other embodiments, the applicator 840 can be attached to a base unit through an umbilical cord. The applicator 840 includes a rechargeable battery 846 that stores energy sufficient for a number of optical pulses, such as, for example, up to 15 optical pulses. A charger contact plate 852 on the applicator 840 engages with the charger 850 in order to recharge the rechargeable battery 846 (see Figure 49B). The applicator 840 can also include a power supply 854.

The applicator 840 can also include a spring 856 and a contact plate 858, which together form a spring-loaded contact plate. The spring-loaded contact plate can ensure a controlled mechanical pressure of the contact plate 858 on the patient's skin 860. In addition, the spring-loaded contact plate can form a system that enables light output from the applicator 840 only when the plate 858 is in contact with patient's skin 860. For example, a sensor or the like can be included in the applicator 840 to sense when the contact plate 858 is in contact with the skin 860, and the applicator 840 can disable the light source of the applicator 840 when the contact plate 858 is not in contact with the patient's skin 860. The contact plate 858 can be made from a transparent material such

as, for example, sapphire. The contact plate 858 can have other features similar to other contact plates described in this specification (such as, for example, cooling features).

In the embodiment of Figures 49A, 49B, and 50, the applicator 840 includes an EMR source 862 and optionally, a reflector 864 and a filter 866. The reflector 864 and filter 866, if used, can be the same as or similar to those set forth in the embodiments above. The EMR source 862 can be, for example, a Xe-flashlamp-based device, as shown in Figure 49A. Other EMR sources 862 can be used in other embodiments. The applicator 840 can also include controls 868 to control the fluence of the light, the filtering of the light through filter 866, and other functions.

The system also includes a patch 844. The role of the patch 844 is two-fold. First, it serves as a container for the topical composition 870 for application through the skin 860. Second, it can feature a highly absorptive optical pattern 872, realized either as a net or as a set of separate "islands" (such as dots). Figure 50 shows an enlarged patch 844 (the applicator 840 is not to scale in Figure 50). Referring to Figure 50, the patch 844 contains a topical medication 870, an adhesive ring 874, an external occlusive film 876, a pattern of optical absorbers 872, and a protective film 878. The topical medication 870 can be any compound, composition, or medicine intended for delivery through the skin 860. For instance, it can be a compound to treat acne.

The pattern of optical absorbers 872 can be made out of inert and biocompatible material to ensure a high absorption of light energy. For example, the optical absorbers 872 can be made from carbon powder. Numerous other types of optical absorbers 872 can also be used in place of or in addition to carbon powder. The pattern of the optical absorbers 872 can vary in different embodiments. In some embodiments, an organized matrix arrangement can be used, while in other embodiments, a less organized or random arrangement of optical absorbers 872 can be used.

The adhesive ring 874 is formed at the bottom of the patch 180 and is used for securing the patch 844 to the skin 860. The adhesive ring 874 can be shaped as a ring with an opening in the middle, although other geometries can also be used. The opening can prevent the adhesive ring 874 from interfering with the operation of the patch 844. That is, the opening will contact the skin 860 and not the adhesive ring 874, preventing the adhesive ring 874 from obstructing in the functionality of the patch 844. The

adhesive ring 874 can be made from any adhesive material. In addition, although this application uses the term adhesive ring, any device for attaching the patch 844 to the skin surface 860 can be used in place of the adhesive ring 874. The protective film 878 covers the bottom of the patch 844 prior to use and is intended to be removed before application. The protective film 878 serves to keep the adhesive ring 874 fresh prior to use and to protect the rest of the patch 180 from contamination. The occlusive film 876 is generally transparent to light 880 and serves to protect the top of the patch 844.

In operation, the patch 844 is brought into contact with the skin 860. In an embodiment for treating acne, the patch 844 can be placed over a portion of skin 860 with an acne lesion 861. The user can then use the applicator 840 to deliver pulses of light 880 to the patch 844. When a pulse of light 880 shines on the patch 844, the optical absorbers 872 absorb the light energy, which results in a rapid temperature elevation. Since the optical absorbers 872 contact the skin surface 860, some of the thermal energy will be conducted to the stratum corneum, creating a corresponding pattern of enhanced permeability channels in the stratum corneum. Thus, penetration of the topical medication 870 into the skin 860 is accelerated, enabling faster effect of the medication. The patch 844 is then left on the skin 860 for a short period of time, for example, up to about two hours. Parameters of the light/patch system are selected in such a way so that no irreversible damage is caused to the stratum corneum; that is, so that integrity of the skin barrier is restored in a short time. The expected benefit is a more rapid improvement in the appearance of the acne lesion or other application.

#### B. Acne treatment device with spatially modulated output

Figures 51A and 51B show a second embodiment of a treatment device for acne (or possibly other conditions). The device is similar to that described above, but the pattern of optical absorbers is created on the output plate of the device, rather than on a separate patch. In this embodiment, no patch is needed, and the topical composition can be applied directly to the skin 860.

Referring to Figure 51A, the applicator 840 of this embodiment can include many of the same components as the embodiment of Figures 49 and 50. For example, the applicator 840 can include a rechargeable battery 846, a charge contact plate 852, a power supply 854, an EMR source 862, a reflector 864, a filter 866, and a contact plate

858 and spring 856. The charge contact plate 852 provides for engagement of the applicator 840 with a charger 850 so that the applicator 840 can be recharged. Each of these components can be the same or similar to those set forth above.

In the embodiment of Figure 51A, the contact plate 858 contains a pattern of optical absorbers 886. In this embodiment, the pattern of optical absorbers 886 is robust enough to withstand multiple treatments. The optical absorbers 886 can be made from any suitable absorbing material, such as, for example, carbon powder. The pattern of optical absorbers 886 can be integrated in the contact plate 858 so that if the optical absorbers 886 are heated up, this heat can warm the skin 860.

In operation, the user can apply a topical compound 884 or medication to the skin 860 over an acne lesion 861. The user can place the contact plate 858 of the applicator 840 in contact with the patient's skin 860 and then use the applicator 840 to deliver pulses of light 880 to the optical absorbers 886. The optical absorbers 886 heat up, creating a pattern of enhanced permeability channels in the stratum corneum. Alternatively, the topical compound 884 can be applied after creation of the pattern of enhanced permeability channels in the stratum corneum.

In an embodiment using a flash lamp, the technical specifications of the treatment devices of Figures 49 through 51 can be as summarized in Table E1 below. These embodiments can be used for a number of applications, including skin diseases and cosmetic treatments.

**Table E1**

| <b>Specification</b>             | <b>Symbol</b>                    | <b>Value</b> | <b>Units</b>      |
|----------------------------------|----------------------------------|--------------|-------------------|
| Incident Fluence                 | Finc                             | 1 - 25       | J/cm <sup>2</sup> |
| Wavelength Range (of EMR source) | $\lambda_{\min}, \lambda_{\max}$ | 400 - 2000   | nm                |
| Spot Size (of optical absorbers) | SS                               | 1 – 50 dia.  | mm                |
| Pulse width (of EMR source)      | PW                               | 1 - 1000     | ms                |
| Lifetime                         | Tlife                            | 10-10000     | pulses            |
| Number of Lamps (of EMR source)  | #lamps                           | 1-10         | #                 |
| Pulse Period (of EMR source)     | T                                | 1 - 10       | sec               |
| Island/mesh Diameter             | ID                               | 10-100       | um                |
| Pattern pitch                    | PP                               | 100-5000     | um                |

## EXAMPLE 7

Treatment of Deep Layer of Tissue

The present invention provides means for creating non-uniform (modulated) temperature profiles (MTP) deep in the dermis and in hypodermis (typically, at depths exceeding 500  $\mu\text{m}$ ). In some embodiments, such profiles result in formation of a pattern (lattice) of islets of damage (LID). Active or passive cooling is applied to epidermal surface in order to prevent epidermal damage. Thus, the technique of the present invention combines advantageous features of non-ablative and fractional techniques. Creation of MTPs leads to improvements in skin structure and texture via the following mechanisms (the list is not exclusive):

1. Lifting and tightening of skin as a result of shrinkage of collagen fibrils subjected to elevated temperature (immediate effect).
2. Lifting and tightening of skin as a result of coagulation of localized areas in the dermis and hypodermis (immediate to short-term effect).
3. Improvement in skin texture as a result of coagulation of localized areas in the dermis and hypodermis (immediate to short-term effect).
4. Promotion of collagen production due to healing response to thermal stress and/or thermal shock (medium- to long-term effect).

A number of other local and systemic pathologies can be treated with the technique:

1. Acne. By selecting the wavelength of the optical radiation to promote preferential absorption of the optical energy by sebum and/or organizing the pattern to target preferentially sebaceous glands, selective destruction of the glands can be achieved.
2. Hypertrophic scars. By inducing tightening and shrinkage in the scar tissue, transformation of the abnormal connective tissue to normal one can be initiated.
3. Odor reduction. By selectively targeting eccrine glands, production of eccrine sweat can be reduced, and its composition can be changed.
4. Non-skin-surface texturing. The technique can be used for organ augmentation (e.g., lips).

5. Cellulite. By changing mechanical stress distribution at the dermis/hypodermis border, the appearance of cellulite can be improved.

It appears that the angular profile in skin is neither Gaussian nor Lambertian. In fact it is close to uniform. In further considerations we used the Gaussian angular profile 90 deg in full width ( $1/e^2$  level). The transverse intensity profile was assumed to be flat.

A source with the blackbody spectrum at 3000 K as halogen lamp, the skin is of type II were simulated. The heat production at the specified depth is normalized to the input light flux so that the resultant value is expressed in  $1/cm$ . The pass bands are 0.9 – 1.3; 0.9 – 1.5; 0.9 – 1.8  $\mu m$ . The depths in tissue are 2 and 3 mm. Therefore, we have 6 variants.

#### Damage profiles.

To evaluate the damage profiles the following model was used: The monochromatic light strikes the skin of type II through sapphire plate 5 mm in thickness. The initial plate temperature is 0 C. The plate surface opposite to the skin is held at fixed temperature 0 C. The light is monochromatic. There are 3 steps: precooling, light treatment, and post cooling. The sapphire plate with dielectric mirror type coating with transparent holes is held in contact with the skin all the time. The irradiance distribution is evaluated using the MC routine, then, the irradiance data are used to evaluate the temperature and damage dynamics. The beam is 7 mm in diameter and the full angle of divergence is 90 deg in the skin.

Under the reasonable choice of the input fluence the damage zone is 1 – 6 mm in diameter that is smaller than the beam diameter. For the 10 s treatment time the depth of the damage zone is 2-2.8 mm (1064 nm), about 2 mm (1270 nm), about 1.5 mm (1700 nm), 1.1 – 1.2 mm (1560 nm) depending on the treatment time. (The larger is the treatment time the deeper is the damage zone). The characteristics of the damage zone are almost independent on the precooling and post cooling times. When using collimated beam instead of divergent one the light flux may be slightly decreased, however, the location and the shape of the damage zone does not change appreciably. The damage zone is almost spherical for 1064 and 1270 nm and becomes squeezed in the vertical direction for 1700 and 1560 nm. It appears that the distance between the spots has to exceed the spot diameter by at least 1.5 mm.

### Experimental Results

A tungsten halogen lamp-based device with appropriate filters provides output radiation between 800 nm and 3.0  $\mu\text{m}$  at adjustable fluences and pulse widths from 1 to 15 J/cm<sup>2</sup>. This device also has a cooled sapphire window interface through which the radiation is applied that contacts with the sample tissue. The beam diameter is fixed at 8 mm. Full thickness, farm pig skin is prepared and placed on a heated pad to provide approximate temperatures of 35 degrees C at the bottom layer (fat and sub-dermis) with a surface temperature approximately 30 degrees C. The sapphire window is cooled to approximately 10 degrees C via water cooling lines and a chiller. In one experiment, the device is placed in contact with the pig skin for a prescribed precooling period prior to turning on the lamp for treatment.

Figures 51(a-c) demonstrate skin tightening without epidermis damage. A single treatment exposure is then applied in succession to each of the upper-left four squares (Fig. 51b) followed by a treatment to the lower-left four squares (Fig. 51c).

There is a clear distortion of the skin surface (seen by the distortion of the grid lines) that suggests shrinkage as a result of the treatment. LDH staining reveals the extent of thermal damage to the tissue in Figure 52. The damaged zones span 4-5 mm and are 1 mm in thickness just below the epidermal layer. Note that the epidermis is not damaged by the treatment.

### Equivalents.

While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention as defined by the appended claims. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described specifically herein. Such equivalents are intended to be encompassed in the scope of the appended claims.

CLAIMS

What is claimed is:

1. An apparatus for performing a treatment on a target area of a patient's skin, comprising:
  - a) a housing having a portion that defines a target treatment area on the patient's skin when placed in proximity to the patient's skin; and
  - b) an LED bar mounted within the housing for applying optical energy to the target area, wherein the LED bar includes multiple emitters of optical energy for creating treatment islets in the patient's skin.
2. An apparatus for performing a treatment on a target area of a patient's skin, comprising:
  - a) a housing having a portion that defines a target treatment area on the patient's skin when placed in proximity to the patient's skin; and
  - b) a diode laser bar mounted within the housing for applying optical energy to the target area, wherein the diode laser bar includes multiple emitters of optical energy for creating treatment islets in the patient's skin.
3. The apparatus of claim 2, wherein the emitters are spaced apart so that the optical energy is applied in a multitude of sub-areas.
4. The apparatus of claim 3, wherein the emitters are spaced apart by about 50 to 900  $\mu\text{m}$ .
5. The apparatus of claim 2, wherein the emitters emit light in a wavelength range of about 290 to 10,000 nm.
6. The apparatus of claim 5, wherein the emitters emit light in a wavelength range of about 900 to 10,000 nm.



7. The apparatus of claim 5, wherein the emitters have widths of about 50 to 150  $\mu\text{m}$ .
8. The apparatus of claim 5, wherein the diode laser bar is about 1 cm long.
9. The apparatus of claim 8, wherein the diode laser bar is about 1 mm wide.
10. The apparatus of claim 2, wherein the diode laser bar includes 10 to 15 emitters.
11. The apparatus of claim 2, wherein the apparatus includes more than one diode laser bar.
12. The apparatus of claim 11, wherein the apparatus includes five or more diode laser bars.
13. The apparatus of claim 11, wherein the diode laser bars are formed as a stack to create a matrix of treatment islets in the patient's skin when in use.
14. The apparatus of claim 2, further comprising one or both of a cooling element or a heating element attached to the housing.
15. The apparatus of claim 14, wherein the cooling element is disposed between the diode laser bar and the patient's skin when in use.
16. The apparatus of claim 14, wherein the cooling element allows passage therethrough of at least a portion of the optical energy from the diode laser bar.
17. The apparatus of claim 16, wherein the cooling element provides cooling over an entire area of contact with the patient's skin.

18. The apparatus of claim 16, wherein the cooling element creates islets of cooling between the treatment islets.
19. The apparatus of claim 2, wherein the portion of the housing that defines the target treatment area comprises a cooling element, wherein the cooling element is disposed between the diode laser bar and the patient's skin when in use.
20. The apparatus of claim 2, further comprising a speed sensor to measure a speed of movement of the housing across the patient's skin.
21. The apparatus of claim 20, further comprising circuitry to vary the output power of the diode laser bar in response to the speed of movement of the housing across the patient's skin.
22. The apparatus of claim 21, wherein the circuitry regulates an interval between pulses of the diode laser bar so that the interval is inversely proportional to the speed of movement of the housing across the patient's skin.
23. The apparatus of claim 20, wherein the speed sensor is a capacitive imaging array.
24. The apparatus of claim 23, wherein the capacitive imaging array creates images of the treatment area when in use.
25. The apparatus of claim 2, further comprising a motor to move the diode laser bar with respect to the housing.
26. The apparatus of claim 25, further comprising circuitry to control the motor to move the diode laser bar in a direction opposite to a direction of movement of the housing across the patient's skin.

27. The apparatus of claim 2, further comprising one of an imaging, refractive or diffractive optical element disposed in the housing between the diode laser bar and the portion of the housing that defines the target treatment area.
28. The apparatus of claim 2, wherein the housing has a head portion that contacts the skin when in use.
29. The apparatus of claim 28, further comprising a contact sensor to sense when the head is in contact with the patient's skin.
30. The apparatus of claim 2, further comprising a mechanism coupled to the multiple emitters for creating treatment islets in the patient's skin.
31. The apparatus of claim 30, wherein the mechanism is a lens array.
32. The apparatus of claim 30, wherein the mechanism is a bundle of optical fibers, wherein each fiber is connected to at least one emitter.
33. The apparatus of claim 2, wherein the apparatus is a hand held device.
34. The apparatus of claim 2, further comprising an optical element operably coupled to each emitter, wherein the optical element aids in creating the treatment islets.
35. The apparatus of claim 2, further comprising a sensor to sense one or more of contact, speed, and imaging.
36. The apparatus of claim 2, wherein, when in use, outputs from the emitters are within about 50 to 1000 microns of the patient's skin.
37. The apparatus of claim 2, wherein a distance between outputs from the emitters and an output from the housing is within about 50 to 1000 microns.

38. The apparatus of claim 2, wherein a distance between outputs from the emitters and an output from the housing is within about 50 to 1000 microns.
39. A handheld dermatological device, comprising:  
a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin;  
a diode laser bar supported by the housing, the diode laser bar having multiple emitters of optical energy; and  
one of a cooling or heating surface operably connected to the housing, wherein the cooling or heating surface touches the person's skin during use, and wherein output radiation from the diode laser bar passes through the cooling surface to produce treatment islets in the target treatment area.
40. The handheld dermatological device of claim 39, wherein the cooling or heating surface is a sapphire plate.
41. The handheld dermatological device of claim 39, further comprising a diffractive optical element disposed in an optical path between the diode laser bar and the cooling or heating surface for focusing the output radiation.
42. The handheld dermatological device of claim 39, wherein the emitters are spaced apart so that the optical energy is applied in a multitude of sub-areas in the person's skin, with a substantial portion of the target area between the sub-areas remaining unaffected.
43. An apparatus for performing a treatment on a target area of a patient's skin, comprising a light emitting assembly for applying optical energy to the target area, the light emitting assembly including a diode laser bar with multiple emitters of optical energy, wherein the optical energy is applied in a multitude of sub-areas, with a substantial portion of the target area between the sub-areas remaining unaffected.

44. The apparatus of claim 43, further comprising a heating element attached to the light emitting assembly, wherein the heating element is disposed between the light emitting assembly and the target area of the patient's skin and is in contact with the target area when the apparatus is in use to heat the target area, the heating element allowing passage therethrough of at least a portion of the optical energy from the light emitting assembly.

45. The apparatus of claim 43, further comprising a cooling element attached to the light emitting assembly, wherein the cooling element is disposed between the light emitting assembly and the target area of the patient's skin and is in contact with the target area when the apparatus is in use to dissipate heat from the target area, the cooling element allowing passage therethrough of at least a portion of the optical energy from the light emitting assembly.

46. The apparatus of claim 45, wherein the cooling element is made out of sapphire or diamond.

47. The apparatus of claim 45, wherein the cooling element is made out of a material that is optically transparent.

48. The apparatus of claim 43, wherein the light emitting assembly comprises multiple diode laser bars in a stacked arrangement.

49. The apparatus of claim 48, wherein the multiple diode laser bars emit radiation of different wavelengths.

50. The apparatus of claim 43, wherein the optical energy source is in a hand piece.

51. The apparatus of claim 43, wherein the optical energy source is in a separate base unit.

52. The apparatus of claim 43, wherein the optical energy source emits light in a wavelength range of about 290 to 10,000 nm.
53. The apparatus of claim 43, wherein, when in use, outputs from the emitters are within about 50 to 1000 microns of the patient's skin.
54. The apparatus of claim 43, wherein the light emitting assembly includes a housing for the diode laser bar, wherein the housing having a output plate for placement in close proximity to the patient's skin when in use, wherein a distance between the outputs from the emitters and an output area of the output plate is within about 50 to 1000 microns.
55. The apparatus of claim 43, further comprising an element for creating islets of treatment selected from the group consisting of a diffractive optical element and a mask.
56. An apparatus for performing a treatment on a target area of a patient's skin by applying optical energy on the target area, comprising:
- a) an optical energy source;
  - b) an applicator movable to a position proximate the target area of the patient's skin for applying optical energy to the target area; and
  - c) one or more optical fibers for transmitting optical energy from the optical energy source to the applicator;
- wherein the applicator includes a mechanism for delivering optical energy onto the target area, and wherein the apparatus creates islets of treatment.
57. An apparatus as in claim 56, wherein the mechanism for delivering optical energy is a total internal reflection element.
58. An apparatus as in claim 56, wherein the optical energy source is selected from a group consisting of a LED, a laser, a diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, and a fluorescent lamp.
59. An apparatus as in claim 56, wherein the applicator is a hand piece.

60. An apparatus as in claim 56, wherein the optical energy source is located in the hand piece.
61. An apparatus as in claim 56, wherein the optical energy source is located in a separate base unit.
62. An apparatus as in claim 56, wherein the optical energy source creates damage islets.
63. An apparatus as in claim 56, wherein each optical fiber provides a separate beam of light.
64. An apparatus as in claim 56, further comprising a re-imaging optical train.
65. A handheld dermatological device, comprising:  
a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin; and  
a plurality of optical fibers within the housing to couple radiation from a radiation source through the hand piece to the person's skin, wherein the optical fibers are spaced apart to output radiation to create treatment islets.
66. The handheld dermatological device of claim 65, wherein the radiation source is located within the hand piece.
67. The handheld dermatological device of claim 65, wherein the radiation source is located outside the hand piece.
68. An apparatus for performing a treatment on a target area of a patient's skin, comprising:

a) a light emitting assembly for applying optical energy to the target area of the patient's skin, the light emitting assembly including a head portion movable across the target area of the patient's skin and an optical energy source for outputting optical energy from the light emitting assembly, the source being movably mounted relative to the head;

b) a sensor for determining the speed of movement of the head portion across the target area of the patient's skin; and

c) circuitry in communication with the sensor for controlling movement of the source relative to the head portion based on the speed of movement of the head portion across the target area of the patient's skin, such that islets of treatment are formed on the target area of the patient's skin.

69. An apparatus as in claim 68, wherein the circuitry controls movement of the source such that the source is kept generally stationary relative to the target area as the head portion is moved relative to the target area.

70. An apparatus as in claim 68, wherein the circuitry controls movement of the source such that the source is moved in a direction generally opposite the direction of movement of the head portion from a first position in the head portion to a second position in the head portion at generally the same speed as the movement of the head portion, and when the source reaches the second position, it is returned to the first position.

71. An apparatus as in claim 68, wherein the source is mounted on a linear translator in the head portion.

72. An apparatus as in claim 68, wherein the source is mounted on a rotatable cylindrical shaft.

73. An apparatus as in claim 68, wherein the optical energy source is selected from a group consisting of a LED, a laser, a diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, and a fluorescent lamp.



74. An apparatus as in claim 68, wherein the sensor consists of one or more capacitive imaging arrays.
75. An apparatus as in claim 74, wherein the capacitive imaging array images treated area for real-time or later viewing.
76. An apparatus as in claim 74, wherein the capacitive imaging arrays are positioned on front and back-sides of the head portion so head portion can be moved forward and backward.
77. An apparatus as in claim 68, wherein the sensor is a wheel with a rotation frequency meter.
78. An apparatus as in claim 77, wherein the sensor is an optical encoder.
79. An apparatus as in claim 68, wherein the light emitting assembly can be entirely in a hand piece or have a source in a separate base unit.
80. An apparatus as in claim 68, further comprising an element to create islets of treatment, wherein the element is selected from a group consisting of a diffractive optical element, a filter, and a mask.
81. An apparatus as in claim 68, further comprising a cooling element in contact with the skin.
82. An apparatus as in claim 81, wherein the cooling element is made out of sapphire or diamond.
83. An apparatus for performing a treatment on a target area of a patient's skin, comprising:  
a) a light emitting assembly including a non-coherent light source for applying optical energy to the target area; and

b) a plurality of light directing elements at an output end of the light emitting assembly, wherein the light directing elements are shaped so that substantially no light will pass through the output end when the output end is not in contact with the patient's skin, wherein the light directing elements create treatment islets in the patient's skin.

84. An apparatus as in claim 83, wherein the light source is selected from a group of a linear flash lamp, an arc lamp, an incandescent lamp, and a halogen lamp.

85. An apparatus as in claim 83, wherein one or more of the light directing elements is selected from a group consisting of an array of pyramids, cones, hemispheres, grooves, and prisms.

86. A dermatological device, comprising:

a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin when in contact with the person's skin;

a light path between an energy source and the head portion;

a plurality of light directing elements to direct light from the energy source, wherein the light directing elements are shaped so that substantially no light will pass through the head portion when the head portion is not in contact with the person's skin, wherein the light directing elements create treatment islets in the patient's skin.

87. An apparatus for performing a treatment on a target area of a patient's skin, comprising:

a) a light emitting assembly including a non-coherent light source for applying optical energy to the target area; and

b) an element at an output end of the light emitting assembly comprising an optically diffusive surface with optically transmissive spots for output light spatial modulation.

88. An apparatus as in claim 87, wherein the light source is selected from a group of a linear flash lamp, an arc lamp, an incandescent lamp, and a halogen lamp.

89. An apparatus as in claim 87, further comprising one or more of the light directing elements selected from a group consisting of a reflector, a filter, and a light duct.

90. An apparatus as in claim 87, wherein one or more of the light directing elements is selected from a group consisting of an array of pyramids, cones, hemispheres, grooves, and prisms.

91. An apparatus as in claim 87, wherein the optically transmissive spots can have various shapes.

92. An apparatus as in claim 91, wherein the shapes of the optically transmissive spots are one or more of circles, slits, rectangles, ovals, or irregular shapes.

93. A light emitting assembly for use in performing a treatment on a target area of a patient's skin, comprising:

- a) a non-coherent light source; and
- b) a light guide for transmitting optical energy from the light source to the target area, the light guide comprising a bundle of optical fibers, wherein the bundle of optical fibers create islets of treatment on the patient's skin.

94. The light emitting assembly as in claim 93, wherein the light guide is made from a bundle of fibers doped with ions of rare earth metals.

95. The light emitting assembly as in claim 93, wherein the fibers are wrapped around the light source.

96. The light emitting assembly as in claim 93, wherein a micro lens is attached to output end of the light guide.

97. The light emitting assembly as in claim 93, wherein the light source is selected from a group of a linear flash lamp, an arc lamp, an incandescent lamp, and a halogen lamp.
98. The light emitting assembly as in claim 93, further comprising a filter between the light source and the light guide.
99. The light emitting assembly as in claim 93, further comprising a reflector partially surrounding the light source.
100. A light emitting assembly for use in performing a treatment on a target area of a patient's skin, comprising:  
a plurality of non-coherent light sources; and  
a plurality of light guides, each light guide transmitting optical energy from a different one of the light sources to the target area, the plurality of light guides providing light spatial modulation.
101. The light emitting assembly as in claim 100, wherein the output ends of the plurality of light guides create islets of treatment on the patient's skin.
102. An apparatus as in claim 100, wherein the light source is selected from a group of a linear flash lamp, an arc lamp, an incandescent lamp, and a halogen lamp.
103. An apparatus as in claim 100, further comprising a filter between the light source and the light guide.
104. An apparatus as in claim 100, further comprising a reflector partially surrounding the light source.
105. An apparatus for performing a treatment on a target area of a patient's skin, comprising:

a) a light emitting assembly for applying optical energy from an optical energy source to the target area; and

b) a mask attached to the light emitting assembly, the mask positioned between the optical energy source and the target area when the apparatus is in use, the mask comprising one or more dielectric layers and including a plurality of openings therethrough for passage of optical energy from the optical energy source to the target area.

106. The apparatus of claim 105, wherein the dielectric layers have a high reflectance over a spectral band emitted by the optical energy source.

107. The apparatus of claim 105, wherein the optical energy source is selected from a group consisting of a LED, a laser, a diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, and a fluorescent lamp.

108. The apparatus of claim 105, wherein the openings have various shapes.

109. The apparatus of claim 108, wherein the shapes of the openings are one or more of lines, circles, slits, rectangles, ovals, or irregular shapes.

110. The apparatus of claim 105, wherein the openings have identical shapes.

111. The apparatus of claim 105, wherein the edges of the openings are coated with non-reflective coatings.

112. The apparatus of claim 105, further comprising a Fresnel or a refractive lens for angular beam shaping.

113. The apparatus of claim 105, wherein the apparatus includes one of a cooling or heating element for cooling or heating the mask during use.

114. The apparatus of claim 113, wherein the cooling element cools the patient's skin when in use.
115. The apparatus of claim 105, wherein the cooling element cools light emitting assembly.
116. The apparatus of claim 105, wherein the cooling element cools components of the apparatus when in use.
117. The apparatus of claim 105, further comprising a waveguide for homogenization of a light beam from the optical energy source.
118. The apparatus of claim 105, further comprising a temperature monitoring mechanism for monitoring the temperature of the target area (or the waveguide).
119. The apparatus of claim 118, wherein the optical energy is in the infrared band.
120. The apparatus of claim 119, wherein the optical energy is in the near infrared band.
121. The apparatus of claim 119, wherein optical energy is applied with a pulse width of 100 fsec to 1 sec.
122. A dermatological device, comprising:  
a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin;  
a light path between an energy source and the head portion; and  
a mirror with holes in it, wherein the mirror is within the light path and the holes allowing for passage of optical energy from the energy source to the target treatment area.

123. A dermatological device, comprising:

a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin; and

a light path between a laser energy source and the head portion, wherein the laser energy source includes a reflector, and wherein an output end of the reflector includes areas of decreased reflectivity relative to the reflectivity of the remainder of the reflector, wherein the areas of decreased reflectivity create treatment islets when in use.

124. The dermatological device of claim 123, wherein the areas of decreased reflectivity function as holes allowing for passage of optical energy from the laser energy source to the target treatment area.

125. An apparatus for performing a treatment on a target area of a patient's skin beneath a skin fold, comprising two light emitting assemblies for applying optical energy to the target area, said light emitting assemblies oriented to emit light beams that intersect at said target area of the patient's skin from generally opposite sides of the skin fold.

126. An apparatus as in claim 125, wherein the light emitting assemblies can include an LED, laser, diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, or a fluorescent lamp.

127. An apparatus as in claim 125, further comprising a mechanism for creating islets of treatment with the optical energy.

128. An apparatus as in claim 127, wherein the mechanism for creating islets of treatment is selected from one or more of a diffractive optical element, a mask, or a filter.

129. A method for performing a treatment on a target area of a patient's skin beneath a skin fold, comprising:

lifting the patient's skin to form a skin fold; and  
applying light beams from generally opposite sides of said skin fold such that said light beams intersect at said target area of the patient's skin.

130. A method as in claim 129, further comprising creating islets of treatment with the light beams.

131. An apparatus for performing a treatment on a target area of a patient's skin, comprising:

a skin lifting implement to lift and stretch the target area of the skin beneath the lifting implement; and

a light emitting assembly for applying optical energy to the target area, said light emitting assemblies oriented to emit light toward the patient's skin.

132. The apparatus of claim 131, wherein the skin lifting implement is a vacuum source.

133. A composition for use in performing a treatment on a target area of a patient's skin, comprising a material applicable selectively over portions of the target area of a patient's skin, the material including an absorbing exogenous chromophore, wherein application of optical energy on the material selectively heats the portions of the target area.

134. The composition of claim 133, wherein the composition includes a high concentration of the chromophore.

135. The composition of claim 134, wherein the composition creates treatment islets over the entire treatment area due to the high concentration.



136. The composition of claim 133, wherein the chromophore is dispersed within the composition so that only portions of the composition having the chromophore heat up upon the application of the optical energy.

137. The composition of claim 136, wherein the optical energy can be applied to the entire composition, resulting in only the portions of the composition with the chromophore heating up.

138. The composition of claim 133, wherein the optical energy is created by a source selected from a group consisting of a LED, a laser, a diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, and a fluorescent lamp.

139. A composition of claim 133, wherein the chromophore is carbon, a metal, an organic dye, a non-organic pigment, or a fullerene.

140. A composition of claim 133, wherein the composition is printable using a printing head on the patient's skin.

141. A composition of claim 143, wherein the printing head is within a hand held device including an optical energy source.

142. A composition of claim 133, wherein the composition is arranged in one or more of dots, lines, or irregular shapes.

143. A composition of claim 133, wherein the composition is a mesh of fibers or threads.

144. A substance for use in performing a treatment on a target area of a patient's skin, comprising:

a) a film applicable over the target area of a patient's skin; and

b) a composition containing an absorbing exogenous chromophore, the composition being selectively affixed to portions of the film, wherein application of optical energy on the composition selectively heats the portions of the target area adjacent the composition.

145. A substance of claim 144, wherein the optical energy is created by a source selected from a group consisting of a LED, a laser, a diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, and a fluorescent lamp.

146. A substance of claim 144, wherein the chromophore is carbon, a metal, an organic dye, a non-organic pigment, or a fullerene.

147. A substance of claim 144, wherein the film is an optically clear polymer.

148. A substance of claim 144, wherein light exposure causes exothermic reaction between at least two different components of the composition.

149. A kit for use in performing a treatment on a target area of a patient's skin, comprising:

a material applicable selectively over portions of the target area of a patient's skin, the material including an absorbing exogenous chromophore; and

a light emitting assembly for applying optical energy to the target area of the patient's skin,

wherein application of optical energy from the light emitting assembly on the material heats the exogenous chromophores to selectively heat portions of the target area of the patient's skin.

150. The kit of claim 149, wherein the optical energy has one or more wavelength bands that match the absorption spectrum of the absorbing exogenous chromophore.

151. The kit of claim 149, wherein the material is a patch for application to the patient's skin.

152. The kit of claim 149, wherein the material is a lotion for application to the patient's skin.

153. A dermatological device, comprising:

a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin when in contact with the person's skin; and

a substrate having a plurality of absorbing elements, wherein incident radiation from an energy source heats up the absorbing elements so that the absorbing elements create treatment islets in the stratum corneum of the person's skin.

154. The dermatological device of claim 153, wherein the substrate is a mask that blocks incident radiation in areas of the mask without the absorbing elements.

155. The dermatological device of claim 153, wherein the mask is formed on a contact plate.

156. The dermatological device of claim 155, wherein the contact plate is a cooling plate.

157. The dermatological device of claim 155, wherein the contact plate forms the head portion of the housing.

158. The dermatological device of claim 153, wherein the absorbing elements are carbon.

159. The dermatological device of claim 153, wherein the energy source is in the housing.

160. The dermatological device of claim 153, wherein the energy source is a base unit that is separate from the housing.

161. A dermatological delivery device, comprising:

a substrate having a plurality of absorbing elements, wherein incident radiation from an energy source heats up the absorbing elements so that the absorbing elements create treatment islets in the stratum corneum of a person's skin; and

a composition contained on at least one side of the substrate, wherein, after removal of the substrate, at least a substantial portion of the composition remains on the person's skin.

162. The dermatological delivery device of claim 161, wherein a portion of the composition penetrates the stratum corneum of the person's skin upon the creation of the treatment islets.

163. A light emitting assembly for use in performing a treatment on a target area of a patient's skin, comprising:

a) a solid state laser;

b) a fiber bundle for receiving optical energy from the laser, wherein the fiber bundle spatially modulates the optical energy from the laser to create islets of treatment on the patient's skin; and

c) focusing optics at an output end of the fiber bundle for projecting optical energy from each fiber of the fiber bundle onto the target area.

164. The light emitting assembly as in claim 163, wherein the laser active rod is made of garnet doped with rare earth ions.

165. The light emitting assembly as in claim 163, wherein the focusing optics comprises a micro lens array.

166. A light emitting assembly for use in performing a treatment on a target area of a patient's skin, comprising:

- a) a solid state laser;
- b) a fiber bundle for receiving optical energy from the laser; and
- c) focusing optics at an output end of the fiber bundle for projecting optical energy from each fiber of the fiber bundle onto the target area, wherein the focusing optics spatially modulates the optical energy from the laser to create islets of treatment on the patient's skin.

167. A light emitting assembly for use in performing a treatment on a target area of a patient's skin, comprising:

- a) a solid state laser;
- b) a phase mask including a plurality of openings for propagating emission from the laser; and
- c) focusing optics at an output end of the phase mask to provide light spatial modulation on the target area.

168. The light emitting assembly as in claim 167, wherein the phase mask creates islets of treatment on the patient's skin.

169. The light emitting assembly as in claim 167, wherein the laser active rod is made of garnet doped with rare earth ions.

170. The light emitting assembly as in claim 167, further comprising a reflector near the laser.

171. The light emitting assembly as in claim 167, further comprising an output coupler at the output end of the laser.

172. The light emitting assembly as in claim 167, wherein the focusing optics comprises a micro lens array.

173. A light emitting assembly for use in performing a treatment on a target area of a patient's skin, comprising:

- a) a bundle of fiber lasers; and
- b) focusing optics at an output end of the bundle to focus emission of each laser onto the target area, wherein the bundle of fiber lasers and focusing optics create islets of treatment on the patient's skin.

174. The light emitting assembly as in claim 173, wherein the laser active rod is made of garnet doped with rare earth ions.

175. The light emitting assembly as in claim 173, further comprising a reflector at the light source.

176. The light emitting assembly as in claim 173, further comprising an output coupler at the output end of the bundle of lasers.

177. The light emitting assembly as in claim 173, wherein the focusing optics comprises a micro lens array.

178. An apparatus for performing a treatment on a target area of a patient's skin, comprising:

- a) a light emitting assembly for applying optical energy to the target area; and
- b) an element attached to the light emitting assembly, the element being disposed between the light emitting assembly and the target area of the patient's skin when the apparatus is in use, the element comprising a reflective material to reflect optical energy from the light emitting assembly back to the light emitting assembly and openings in the reflective material to allow passage therethrough of optical energy from the light emitting assembly.

179. An apparatus as in claim 178, wherein the light emitting assembly includes a source selected from a group consisting of a LED, a laser, a diode laser bar, a radiant lamp, a halogen lamp, an incandescent lamp, an arc lamp, and a fluorescent lamp.

180. An apparatus as in claim 178, wherein the light emitting assembly is surrounded by reflective material.
181. An apparatus as in claim 178, wherein the light is pumped into a box containing one or more reflective surfaces.
182. An apparatus as in claim 181, wherein the reflective surface is a mirror with holes.
183. An apparatus for performing a treatment on a target area of a patient's skin, comprising:
- a) a light emitting assembly including a light source for applying optical energy to the target area; and
  - b) a plurality of light directing elements at an output end of the light emitting assembly for output light spatial modulation and concentration, wherein the optical energy is applied in a multitude of sub-areas, with a substantial portion of the target area between the sub-areas remaining unaffected.
184. The apparatus of claim 183, wherein the light source is a non-coherent light source.
185. The apparatus of claim 183, wherein the light source is selected from a group of a linear flash lamp, an arc lamp, an incandescent lamp, and a halogen lamp.
186. The apparatus of claim 183, wherein the light directing elements are selected from a group consisting of a reflector, a mask, and a light duct.
187. The apparatus of claim 183, wherein the light directing elements comprise a micro lens array.

188. The apparatus of claim 183, wherein one or more of the light directing elements is selected from a group consisting of arrays of pyramids, cones, hemispheres, grooves, and prisms.

189. The apparatus of claim 183, wherein the light source is a coherent light source.

190. The apparatus of claim 189, wherein the light source is selected from a group including a solid state laser, a fiber laser, and a dye laser.

191. The apparatus of claim 189, wherein the light source is a laser active rod made of garnet doped with rare earth ions.

192. The apparatus of claim 189, wherein the light source is a bundle of fiber lasers.

193. The apparatus of claim 189, wherein at least one light directing element is at an output end of each fiber laser for output light spatial modulation and concentration.

194. The apparatus of claim 189, wherein the light emitting assembly includes a fiber bundle disposed between the light source and the light direction elements, wherein the fiber bundle receives optical energy from the light source.

195. The apparatus of claim 194, wherein the fiber bundle spatially modulates the optical energy from the light source.

196. The apparatus of claim 195, wherein the light direction elements are focusing optics at an output end of the fiber bundle for projecting optical energy from each fiber of the fiber bundle onto the target area.

197. A dermatological device, comprising:



a housing capable of being manually manipulated to position a head portion of the housing in proximity to a person's skin, the head portion defining a target treatment area on the person's skin when in contact with the person's skin;

a light path between an energy source and the head portion; and

a plurality of light directing elements to focus light from the energy source to create treatment islets in the person's skin.

198. The dermatological device of claim 197, wherein the plurality of light directing elements is a micro-lens array.

199. A method for increasing the permeability of the stratum corneum of a subject to a compound comprising:

applying EMR radiation to a portion of the stratum corneum of said subject to produce a lattice of EMR-treated islets in said portion of the stratum corneum of said subject,

whereby said lattice of EMR-treated islets is heated to a temperature sufficient to increase the permeability of said portion of the stratum corneum to said compound.

200. A method for increasing the permeability of the stratum corneum of a subject to a compound comprising:

treating a portion of the stratum corneum of said subject with an EMR-treatment device that produces a lattice of EMR-treated islets in said portion of the stratum corneum of said subject,

whereby said lattice of EMR-treated islets is heated to a temperature sufficient to increase the permeability of said portion of the stratum corneum to said compound.

201. The method of claim 200 wherein said compound is selected from the group consisting of a therapeutic agent and a cosmetic agent.

202. The method of claim 200 wherein said compound is a therapeutic agent selected from the group consisting of a hormone, a steroid, a non-steroidal anti-inflammatory drug, an anti-neoplastic agent, an antihistamine and an anesthetic agent.

203. The method of claim 200 wherein said compound is a therapeutic agent selected from the group consisting of insulin, estrogen, prednisolone, loteprednol, ketorolac, diclofenac, methotrexate, histamine H1 antagonists, chlorpheniramine, pyrilamine, mepyramine, emedastine, levocabastine and lidocaine.

204. The method of claim 200 wherein said compound is a cosmetic agent selected from the group consisting of a pigment, a reflective agent and a photoprotectant.

205. The method of claim 200 wherein:

said lattice of EMR-treated islets is heated to a temperature sufficient to at least partially melt a crystalline lipid extracellular matrix in said lattice of EMR-treated islets in said portion of the stratum corneum,

whereby permeability of said portion of the stratum corneum to said compound is increased.

206. The method of claim 205 wherein:

said lattice of EMR-treated islets is heated to a temperature of 35-40°C.

207. The method of claim 205 wherein:

said lattice of EMR-treated islets is heated to a temperature of 40-50°C.

208. The method of claim 205 wherein:

said lattice of EMR-treated islets is heated to a temperature of 50-100°C.

209. The method of claim 205 wherein:

said increase in permeability is reversible after treatment with said EMR-treatment device is discontinued.

210. The method of claim 209 wherein:  
said increase in permeability is reversed by crystallization of said lipid extracellular matrix within 2 hours after said treatment is discontinued.
211. The method of claim 205 wherein:  
said increase in permeability is reversed by crystallization of said lipid extracellular matrix within 1 hour after said treatment is discontinued.
212. The method of claim 209 wherein:  
said increase in permeability is reversed by crystallization of said lipid extracellular matrix within 30 minutes after said treatment is discontinued.
213. The method of claim 209 wherein:  
said increase in permeability is reversed by crystallization of said lipid extracellular matrix within 15 minutes after said treatment is discontinued.
214. The method of claim 205 wherein:  
said lattice of EMR-treated islets is heated to a temperature which is not sufficient to coagulate or denature proteins within the lattice of islets.
215. The method of claim 200 wherein:  
said lattice of EMR-treated islets is heated to a temperature sufficient to at least partially evaporate water present in said portion of the stratum corneum,  
whereby permeability of said portion of the stratum corneum to said compound is increased.
216. The method of claim 215 wherein:  
said lattice of EMR-treated islets is heated to a temperature of 100-200°C.
217. The method of claim 215 wherein:

said lattice of EMR-treated islets is heated to a temperature greater than 200°C.

218. The method of claim 200 wherein:

said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 1  $\mu\text{m}$  to 30 mm.

219. The method of claim 218 wherein:

said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 1  $\mu\text{m}$  to 10  $\mu\text{m}$ .

220. The method of claim 218 wherein:

said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 10  $\mu\text{m}$  to 100  $\mu\text{m}$ .

221. The method of claim 218 wherein:

said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 100  $\mu\text{m}$  to 1 mm.

222. The method of claim 218 wherein:

said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 1 mm to 10 mm.

223. The method of claim 200 wherein:

said lattice of EMR-treated islets in said portion of the stratum corneum has a fill factor of 0.01-90%.

224. The method of claim 223 wherein:

said lattice of EMR-treated islets in said portion of the stratum corneum has a fill factor of 0.01-0.1%.

225. The method of claim 223 wherein:

said lattice of EMR-treated islets in said portion of the stratum corneum has a fill factor of 0.1-1%.

226. The method of claim 223 wherein:

said lattice of EMR-treated islets in said portion of the stratum corneum has a fill factor of 1-10%.

227. The method of claim 223 wherein:

said lattice of EMR-treated islets in said portion of the stratum corneum has a fill factor of 10-30%.

228. The method of claim 223 wherein:

said lattice of EMR-treated islets in said portion of the stratum corneum has a fill factor of 30-50%.

229. A method of transdermal delivery of a compound to a subject comprising:

treating a portion of the stratum corneum of said subject with an EMR-treatment device that produces a lattice of EMR-treated islets in said portion of the stratum corneum of said subject,

whereby said lattice of EMR-treated islets is heated to a temperature sufficient to increase the permeability of said portion of the stratum corneum to said compound.

230. The method of any one of claims 200 or 229 further wherein:

a portion of the papillary dermis below said portion of the stratum corneum is not heated to a temperature above 43°C.

231. The method of any one of claims 200 or 229 further wherein:

a portion of the papillary dermis below said portion of the stratum corneum is not heated to a temperature above 40°C.

232. A method for increasing the permeability of the stratum corneum of a subject to a compound comprising:

treating a portion of the stratum corneum of said subject with an EMR-treatment device that produces a lattice of EMR-treated islets in said portion of the stratum corneum of said subject,

wherein said device produces said lattice of EMR-treated islets by delivering EMR energy to endogenous chromophores within said islets, and

whereby said lattice of EMR-treated islets is heated to a temperature sufficient to increase the permeability of said portion of the stratum corneum to said compound.

233. The method of claim 232 wherein:

said endogenous chromophore is selected from the group consisting of water, a lipid or a protein.

234. The method of claim 232 wherein:

said endogenous chromophore is selected from the group consisting of water, melanin, hemoglobin and collagen.

235. The method of claim 232 wherein:

said EMR-treatment device produces said lattice of EMR-treated islets by delivering EMR energy to a lattice of optical islets in said tissue.

236. The method of claim 235 wherein:

said EMR-treatment device produces a multiplicity of EMR beams which deliver EMR energy to a lattice of optical islets in said tissue.

237. A method for increasing the permeability of the stratum corneum of a subject to a compound comprising:

treating a portion of the stratum corneum of said subject with an EMR-treatment device that produces a lattice of thermal islets in said portion of the stratum corneum of said subject,

wherein said device produces said lattice of thermal islets by delivering EMR energy to exogenous EMR-absorbing particles in contact with said portion of the stratum corneum, and

wherein said EMR-absorbing particles transfer heat to said portion of the stratum corneum to produce said lattice of thermal islets.

238. The method of claim 237 wherein:

said exogenous EMR-absorbing particles are present on the surface of the stratum corneum in a spatial array which corresponds to said lattice, and

said exogenous EMR-absorbing particles are heated by a substantially uniform beam of EMR energy from said device.

239. The method of claim 238 wherein:

said exogenous EMR-absorbing particles are present in a film applied to said surface.

240. The method of claim 238 wherein:

said exogenous EMR-absorbing particles are present in a lotion applied to said surface.

241. The method of claim 237 wherein:

said exogenous EMR-absorbing particles are present on the surface of the stratum corneum in a continuous layer, and

said exogenous EMR-absorbing particles are heated by a multiplicity of EMR beams which deliver EMR energy to a spatial array of said particles which corresponds to said lattice of optical islets in said tissue.

242. The method of any one of claims 200-241 wherein said device is a device of any one of claims 1-199.

243. A method for selectively damaging a portion of tissue in a subject comprising:

applying EMR radiation to a portion of tissue of said subject to produce a lattice of EMR-treated islets in said portion of tissue,

whereby said EMR-treated islets absorb an amount of EMR that is sufficient to damage tissue in said EMR-treated islets but that is not sufficient to cause bulk tissue damage.

244. A method for selectively damaging a portion of tissue in a subject comprising: treating a portion of tissue of said subject with an EMR-treatment device that produces a lattice of EMR-treated islets in said portion of tissue,

whereby said EMR-treated islets absorb an amount of EMR that is sufficient to damage tissue in said EMR-treated islets but that is not sufficient to cause bulk tissue damage.

245. The method of claim 244 wherein:

said damage comprises coagulation or denaturation of intracellular or extracellular proteins in said EMR-treated islets.

246. The method of claim 244 wherein:

said damage comprises evaporation of water in said EMR-treated islets.

247. The method of claim 244 wherein:

said damage comprises killing cells in said EMR-treated islets.

248. The method of claim 244 wherein:

said damage comprises ablation of tissue in said EMR-treated islets.

249. The method of claim 244 wherein:

said lattice of EMR-treated islets is heated to a temperature of 35-40°C.

250. The method of claim 244 wherein:

said lattice of EMR-treated islets is heated to a temperature of 40-50°C.



251. The method of claim 244 wherein:  
said lattice of EMR-treated islets is heated to a temperature of 50-100°C.
252. The method of claim 244 wherein:  
said lattice of EMR-treated islets is heated to a temperature of 100-200°C.
253. The method of claim 244 wherein:  
said lattice of EMR-treated islets is heated to a temperature greater than 200°C.
254. The method of claim 244 wherein:  
said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 1  $\mu\text{m}$  to 30 mm.
255. The method of claim 244 wherein:  
said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 1  $\mu\text{m}$  to 10  $\mu\text{m}$ .
256. The method of claim 244 wherein:  
said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 10  $\mu\text{m}$  to 100  $\mu\text{m}$ .
257. The method of claim 244 wherein:  
said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 100  $\mu\text{m}$  to 1 mm.
258. The method of claim 244 wherein:  
said lattice of EMR-treated islets comprises a multiplicity of islets wherein each islet has a maximum dimension of 1 mm to 10 mm.
259. The method of claim 244 wherein:

said lattice of EMR-treated islets has a fill factor of 0.01-90%.

260. The method of claim 244 wherein:

said lattice of EMR-treated islets has a fill factor of 0.01-0.1%.

261. The method of claim 244 wherein:

said lattice of EMR-treated islets has a fill factor of 0.1-1%.

262. The method of claim 244 wherein:

said lattice of EMR-treated islets has a fill factor of 1-10%.

263. The method of claim 244 wherein:

said lattice of EMR-treated islets has a fill factor of 10-30%.

264. The method of claim 244 wherein:

said lattice of EMR-treated islets has a fill factor of 30-50%.

265. The method of claim 244 wherein:

said EMR-treated islets are thermal islets having a minimum depth from the surface of said tissue of 0-4 mm.

266. The method of claim 265 wherein:

said EMR-treated islets have a minimum depth from the surface of said tissue of 0-50  $\mu\text{m}$ .

267. The method of claim 265 wherein:

said EMR-treated islets have a minimum depth from the surface of said tissue of 50-500  $\mu\text{m}$ .

268. The method of claim 265 wherein:

said EMR-treated islets have a minimum depth from the surface of said tissue of 500  $\mu\text{m}$  - 4 mm.

269. The method of any one of claims 265-268 further comprising:  
cooling the surface of said tissue to prevent the formation of thermal islets at said surface.

270. The method of any one of claims 265-268 further comprising:  
cooling the surface of said tissue to prevent the formation of thermal islets from said surface to said minimum depth.

271. The method of claim 244 wherein:  
said portion of tissue is a wart,  
whereby producing said lattice of EMR-treated islets damages tissue of said wart.

272. The method of claim 244 wherein:  
said portion of tissue is a callus,  
whereby producing said lattice of EMR-treated islets damages tissue of said callus.

273. The method of claim 244 wherein:  
said portion of tissue is a sweat gland,  
whereby producing said lattice of EMR-treated islets damages tissue of said sweat gland.

274. The method of claim 276 wherein:  
said sweat gland is associated with body odor,  
whereby damaging tissue of said sebaceous gland reduces said body odor.

275. The method of claim 244 wherein:  
said portion of tissue is a psoriasis plaque,

whereby producing said lattice of EMR-treated islets damages tissue of said psoriasis plaque.

276. The method of claim 244 wherein:

said portion of tissue is a sebaceous gland,

whereby producing said lattice of EMR-treated islets damages tissue of said sebaceous gland.

277. The method of claim 276 wherein:

said sebaceous gland is associated with an acne sore,

whereby damaging tissue of said sebaceous gland reduces said acne sore.

278. The method of claim 244 wherein:

said portion of tissue is fat tissue,

whereby producing said lattice of EMR-treated islets damages said fat tissue.

279. The method of claim 278 wherein:

said fat tissue is associated with cellulite,

whereby damaging said fat tissue reduces said cellulite.

280. A method for reducing pigment in the skin of a subject comprising:

treating a portion of the skin of said subject with an EMR-treatment device that produces a lattice of EMR-treated islets in at least one volume of tissue containing said pigment,

whereby said pigment is destroyed without killing cells including said pigment.

281. A method for reducing pigment in the skin of a subject comprising:

treating a portion of the skin of said subject with a device that produces a lattice of EMR-treated islets in at least one volume of tissue containing said pigment,

whereby cells including said pigment are destroyed.

282. The method of any one of claims 280-281 wherein:  
said pigment is present in a tattoo, port wine stain, birthmark, or freckle.
283. A method for photodynamic therapy of a subject in need thereof, comprising  
treating a portion of tissue of said subject with an EMR-treatment device that  
produces a lattice of EMR-treated islets in a desired treatment area in said subject,  
whereby said EMR-treatment activates a photodynamic agent present in said  
islets.
284. The method of claim 283, wherein said photodynamic agent is administered to  
said subject prior to said treatment.
285. The method of claim 283, wherein said photodynamic agent is selected from the  
group consisting of an antineoplastic agent and a psoralen.

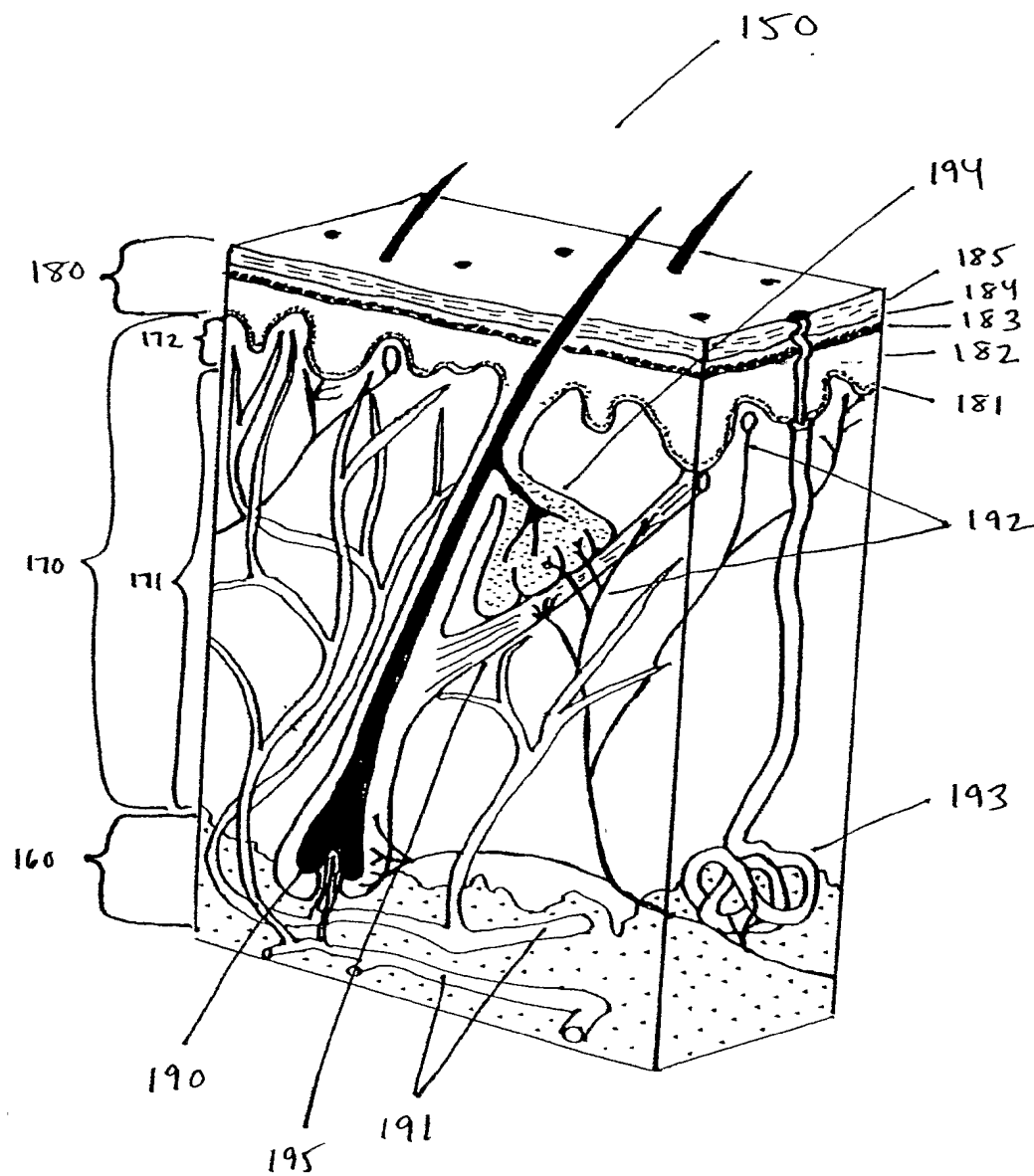


FIGURE 1

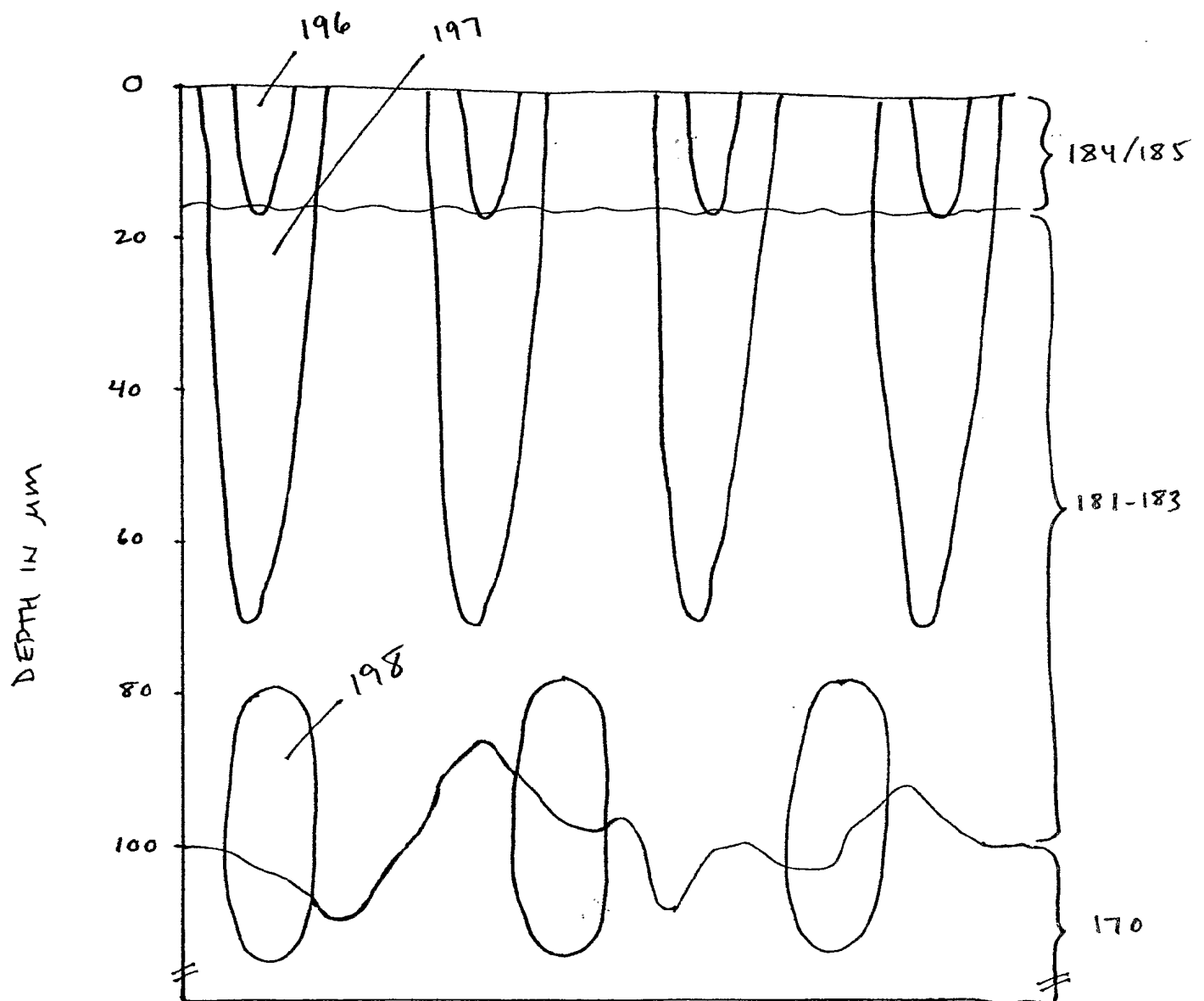


FIGURE 2

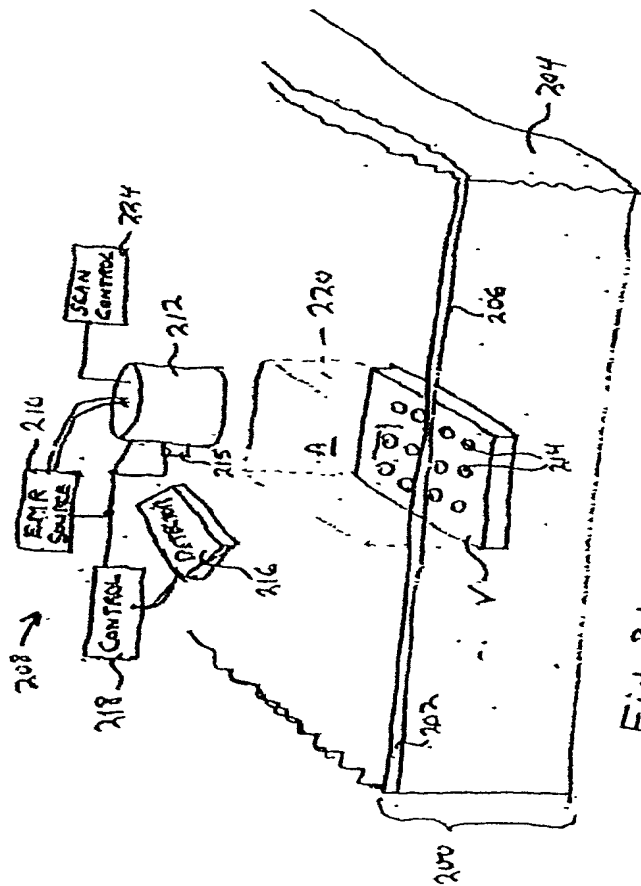


Fig. 3A

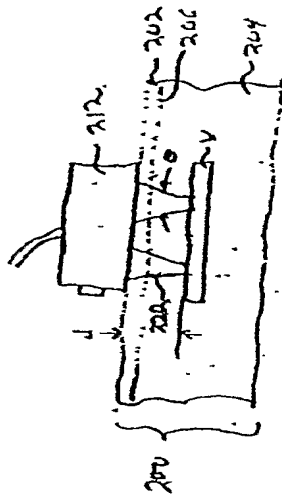


Fig. 3B



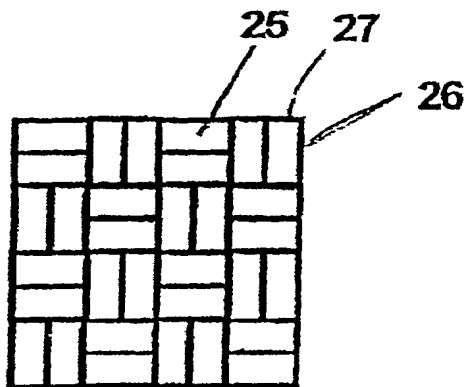


Fig. 4A

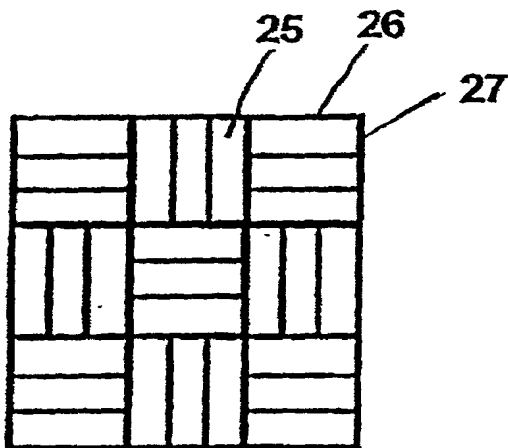


Fig. 4B

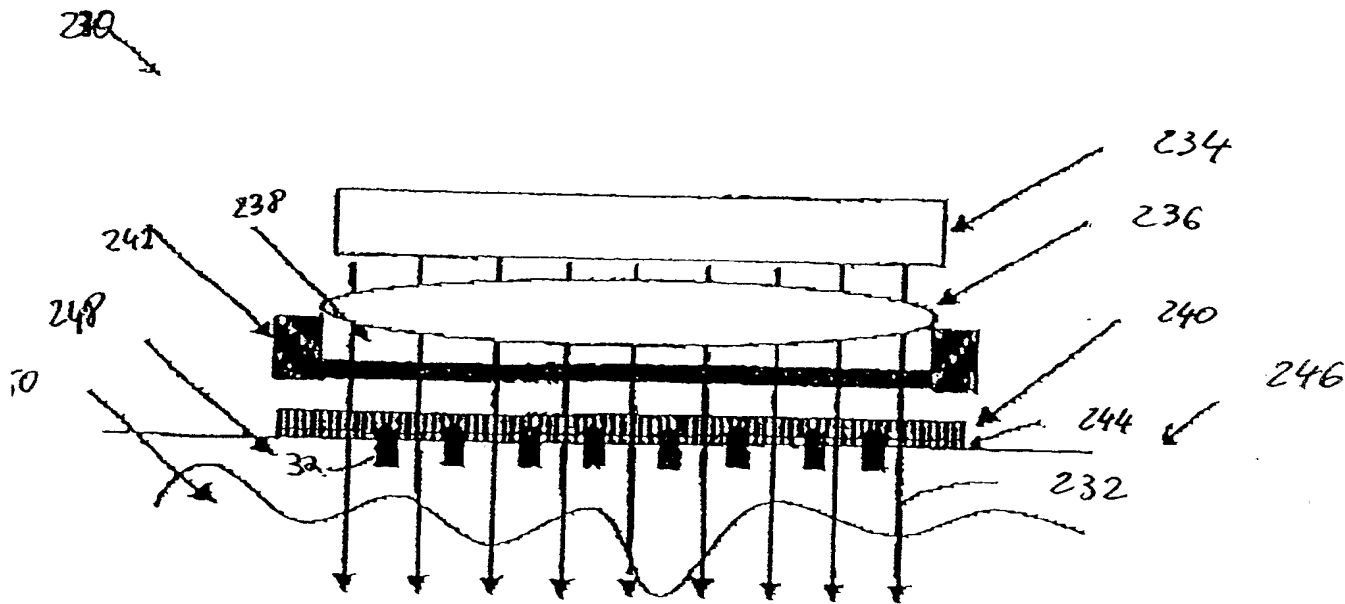


Figure 5.

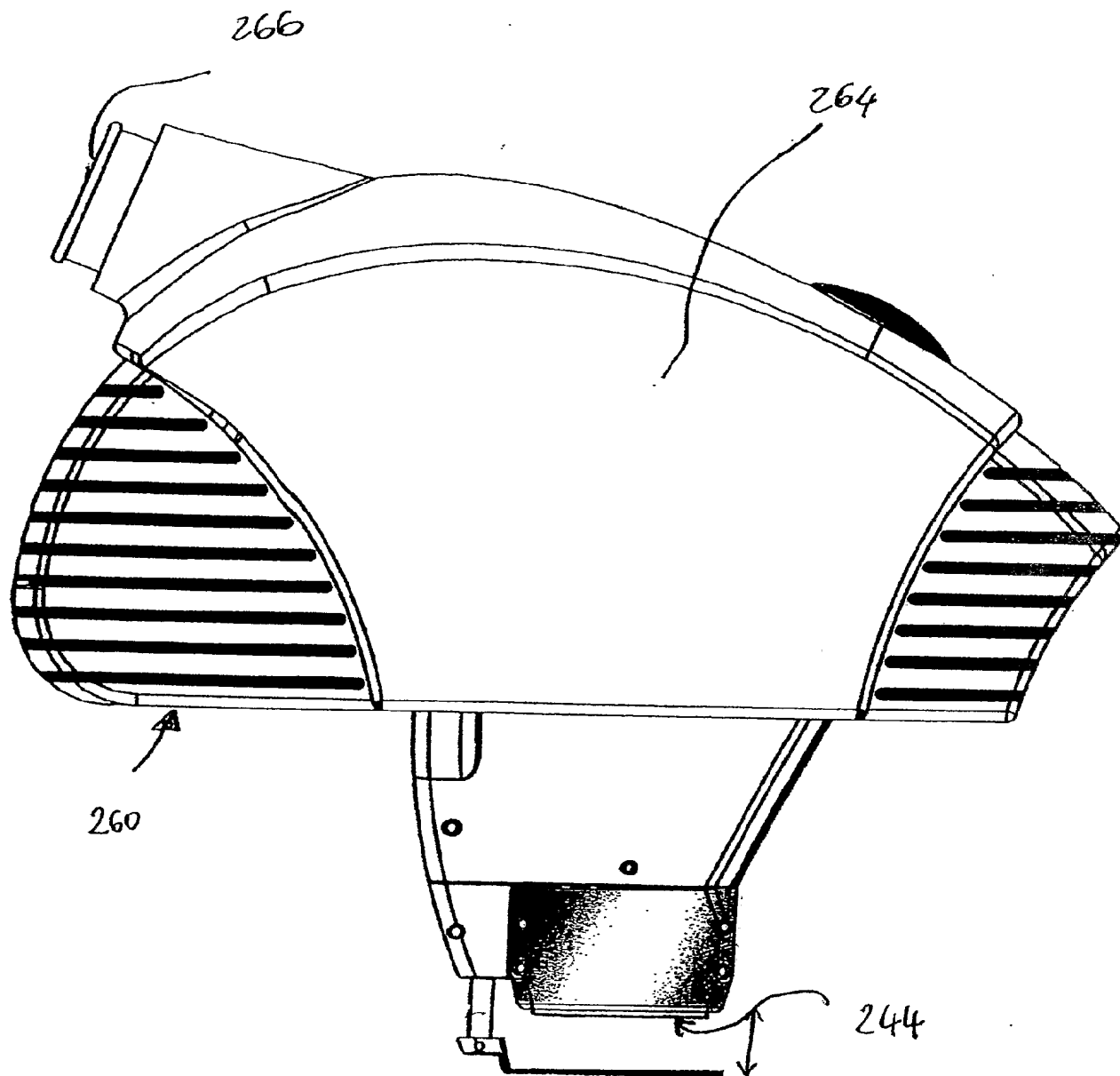


Figure 6

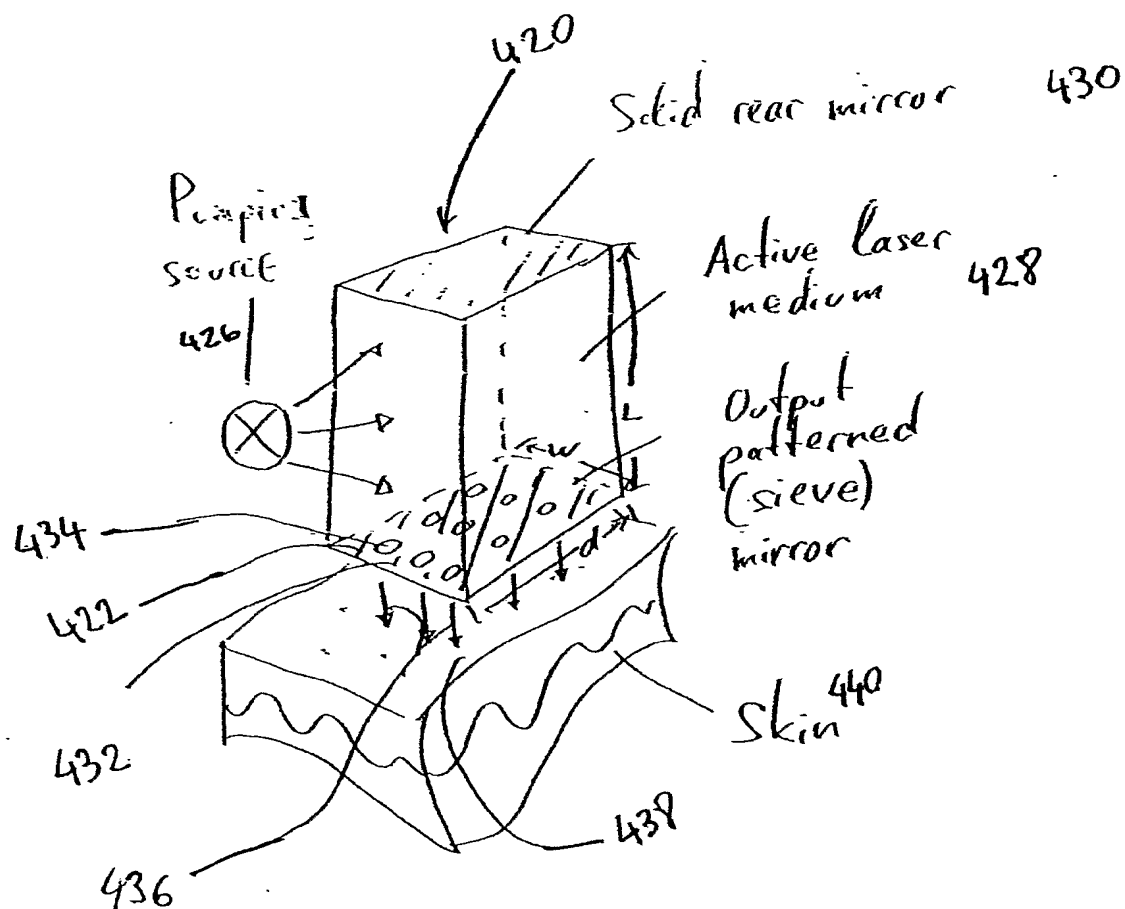


Fig. 7

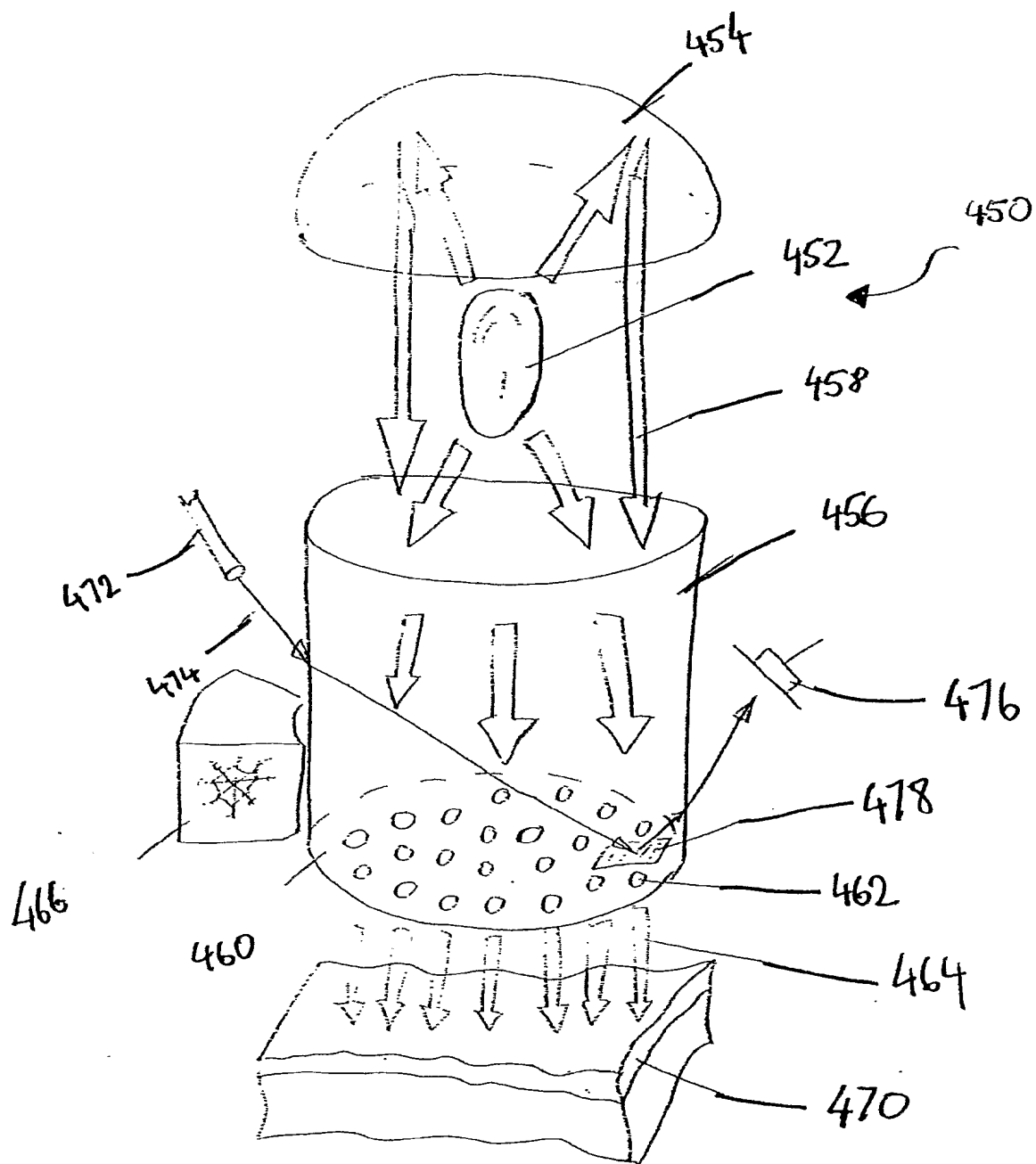
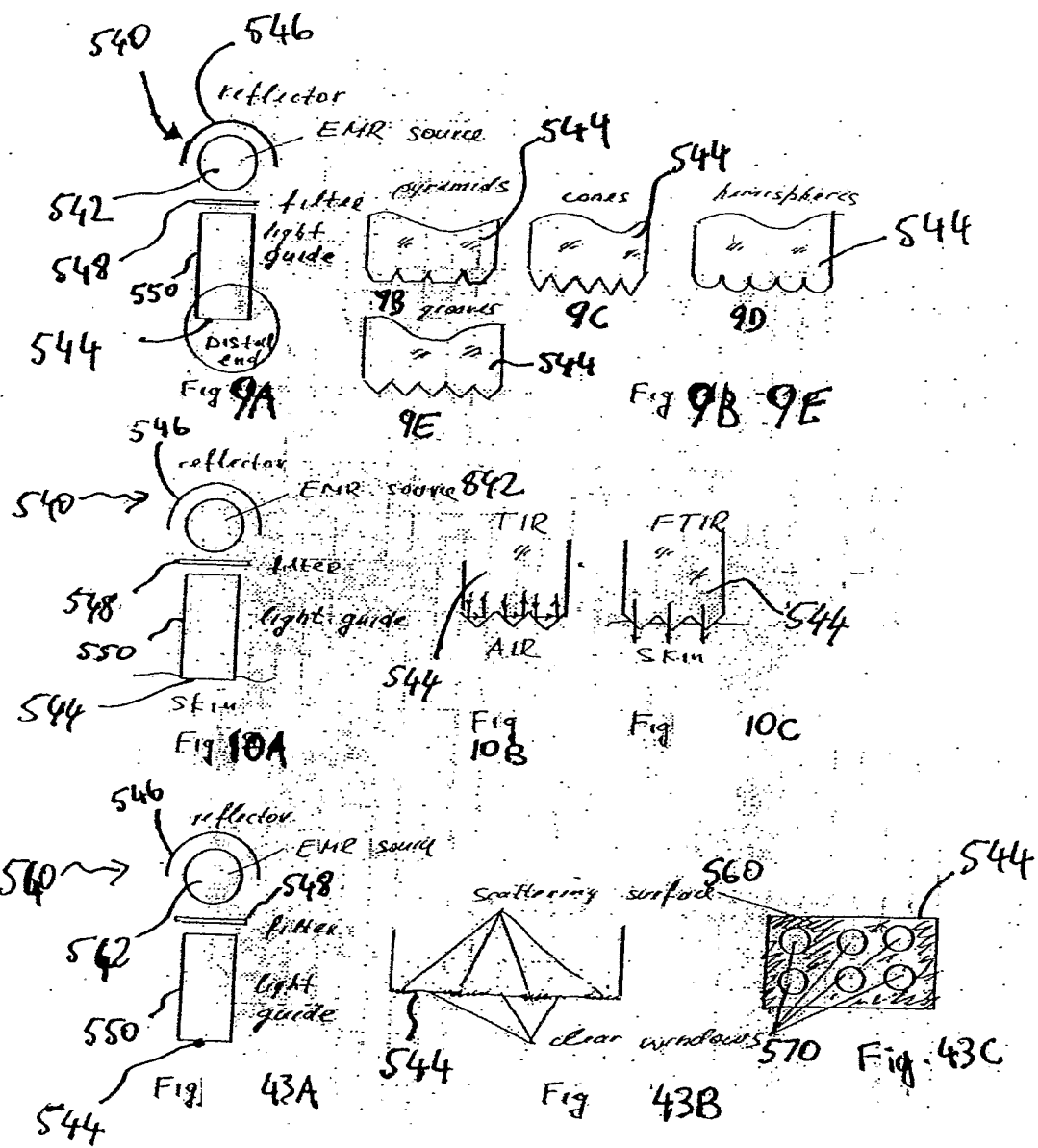


Fig.

8



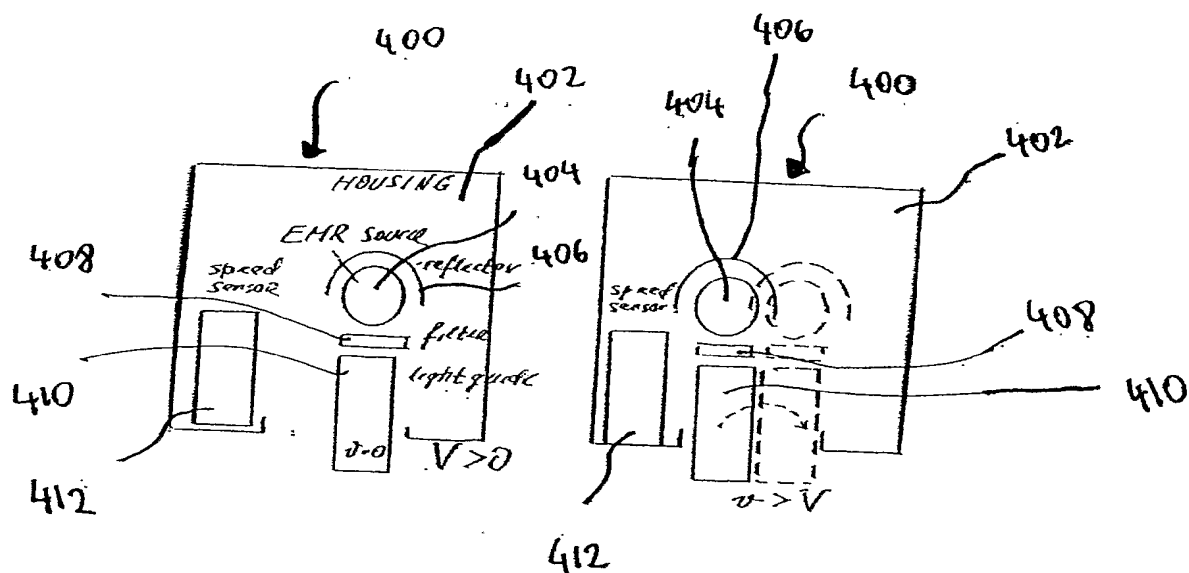


Fig. 41A

Fig. 41B

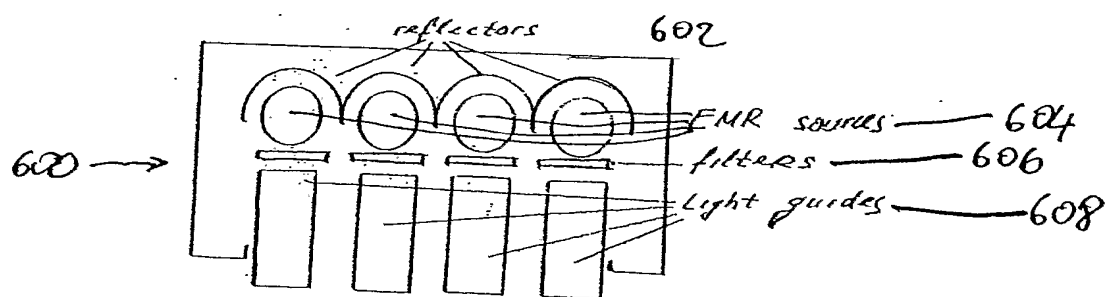


Fig. 11

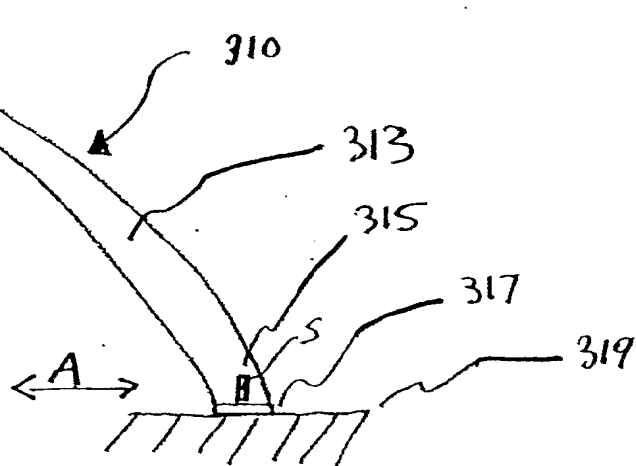


Figure 12A  
[310-325]

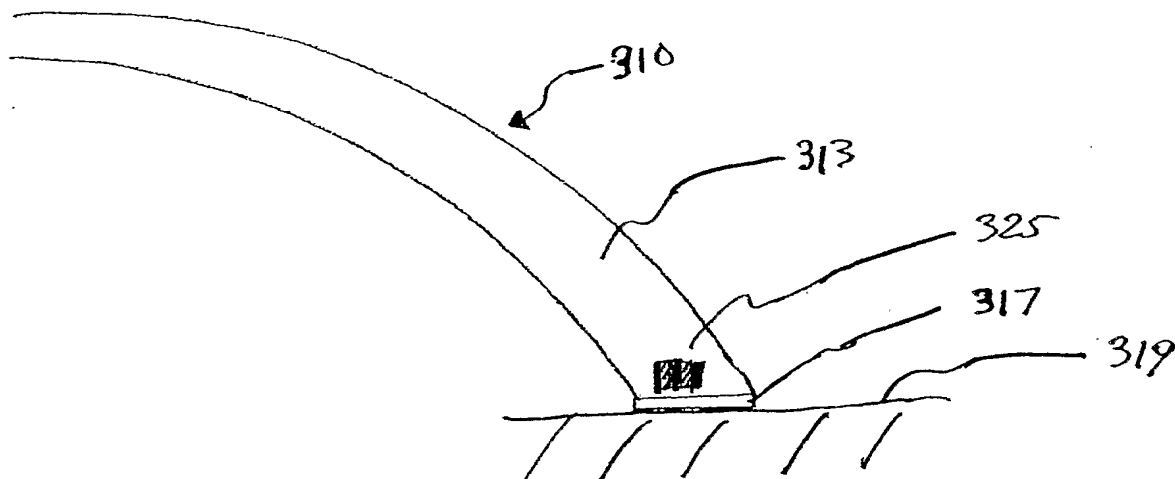
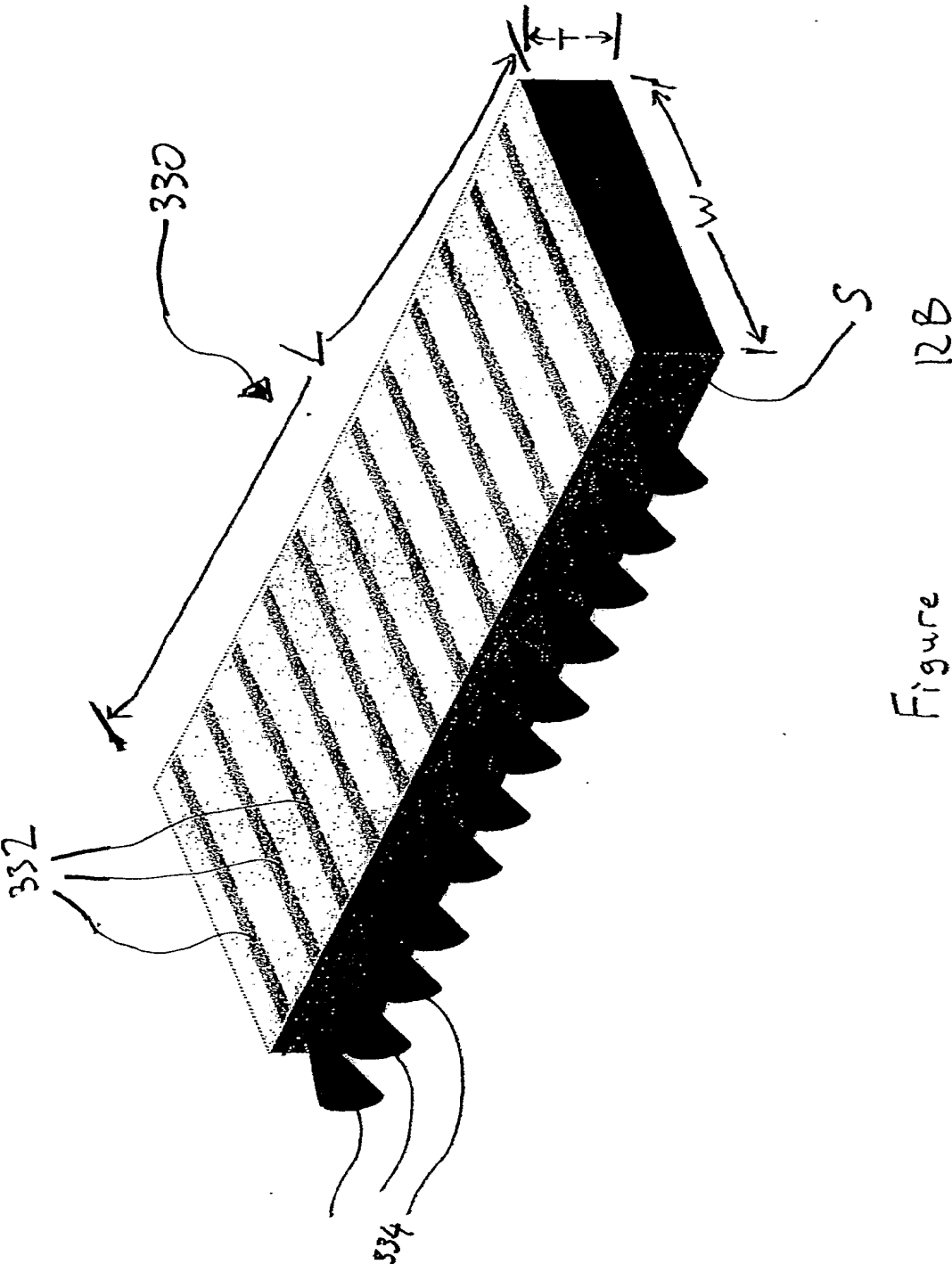


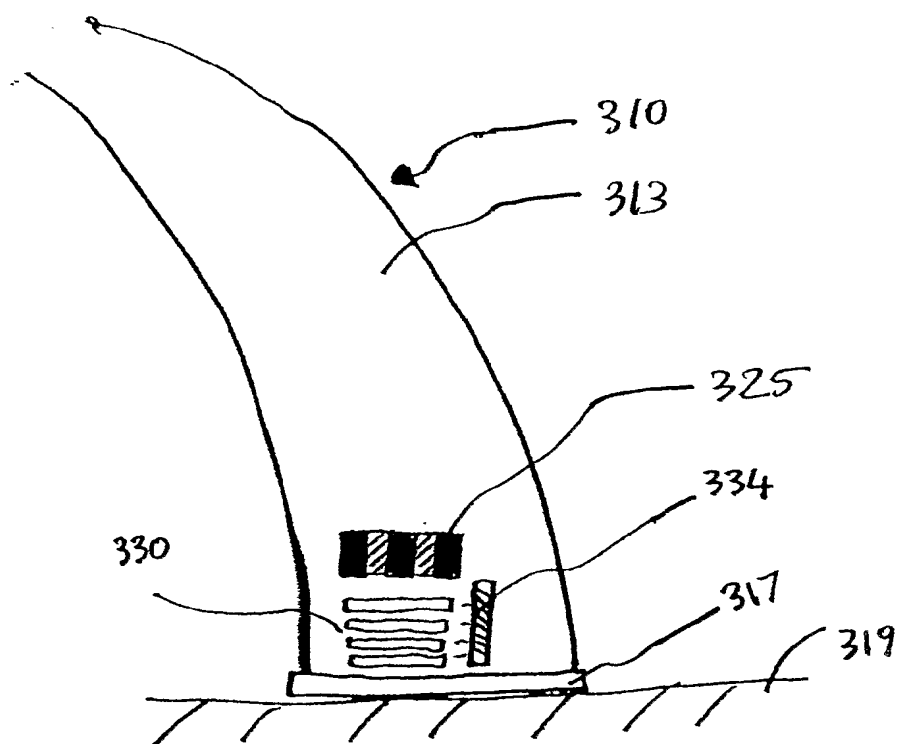
Figure 12C





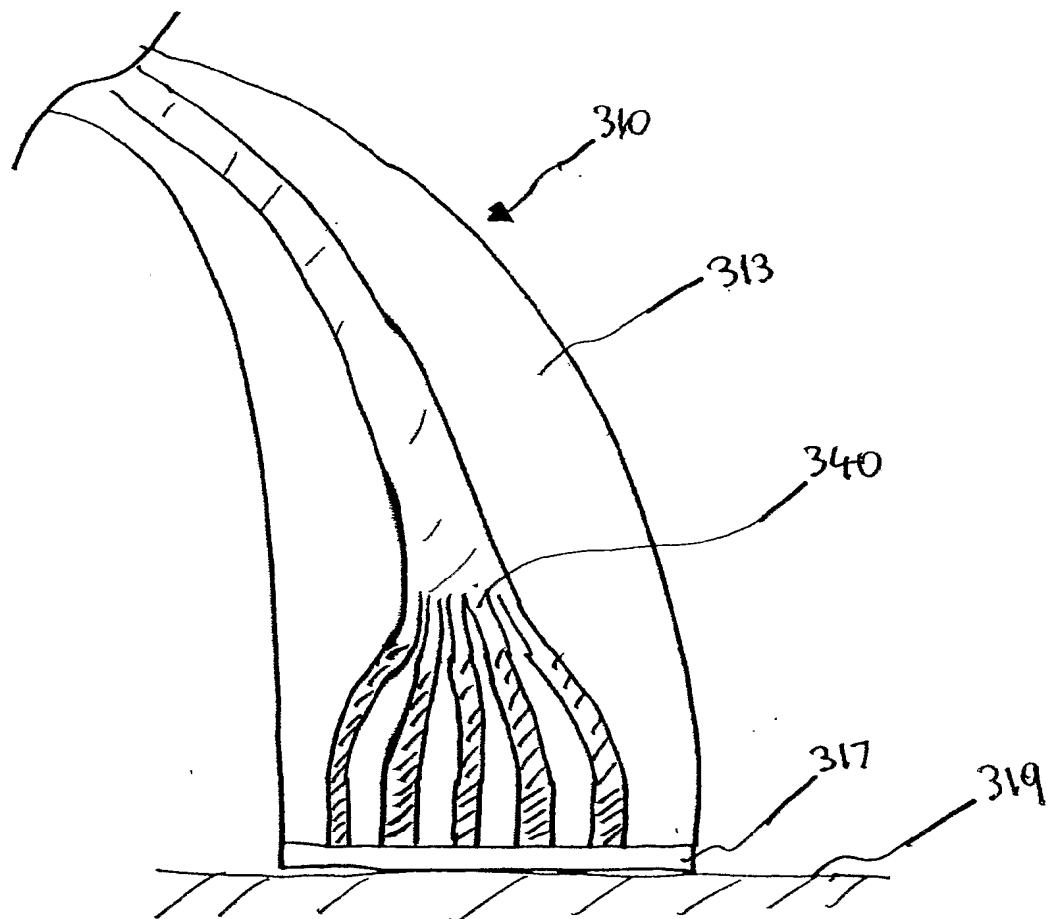
Figure

12B



Figure

12D



Figure

12E

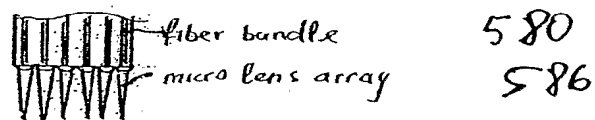
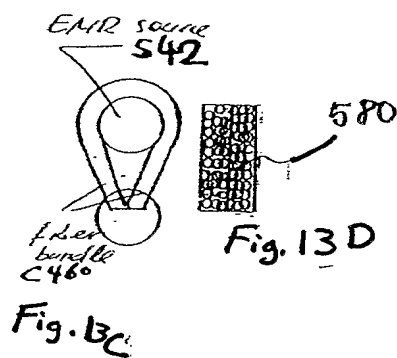
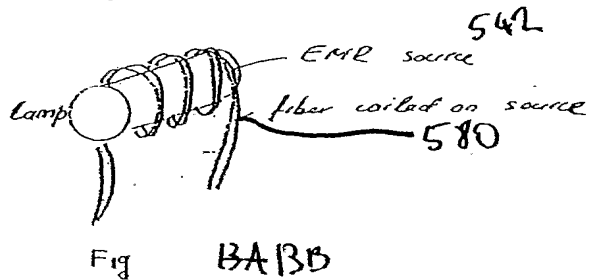
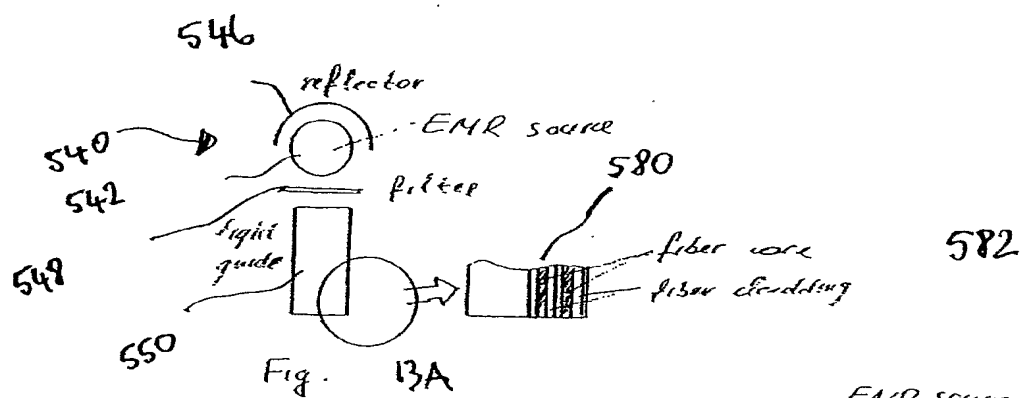
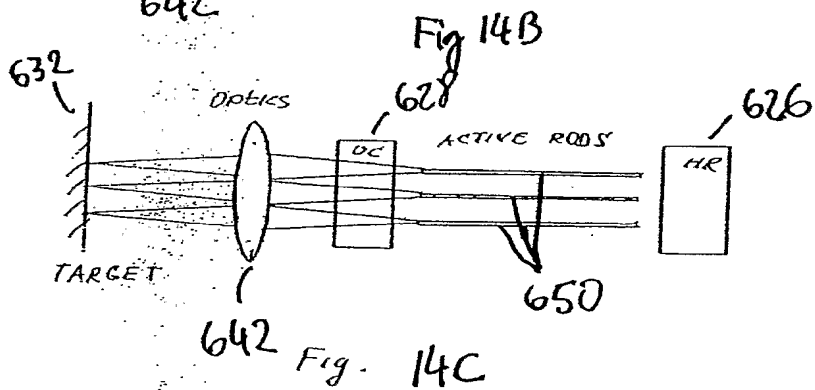
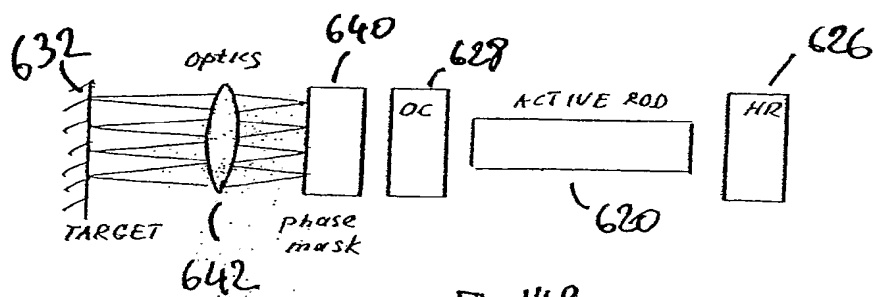
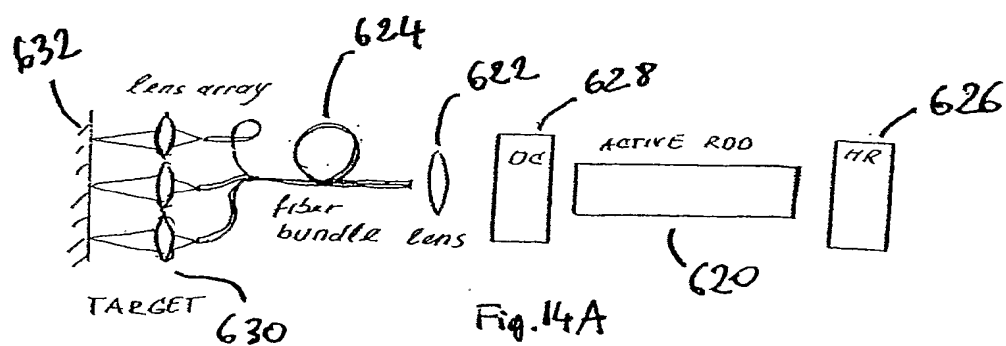


Fig. 13E



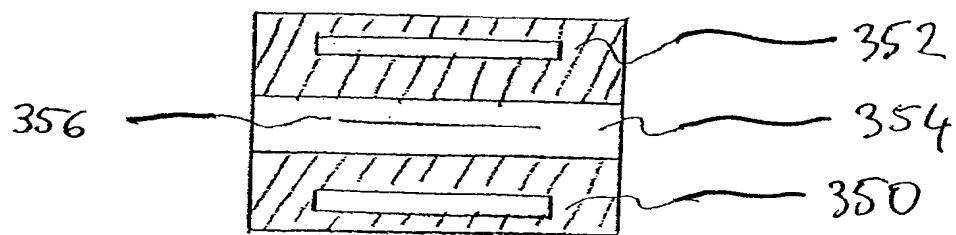


Figure 15

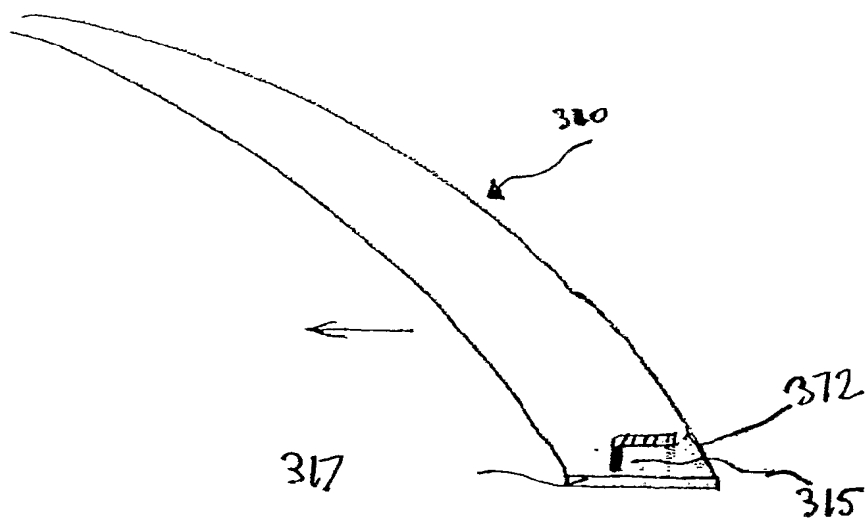
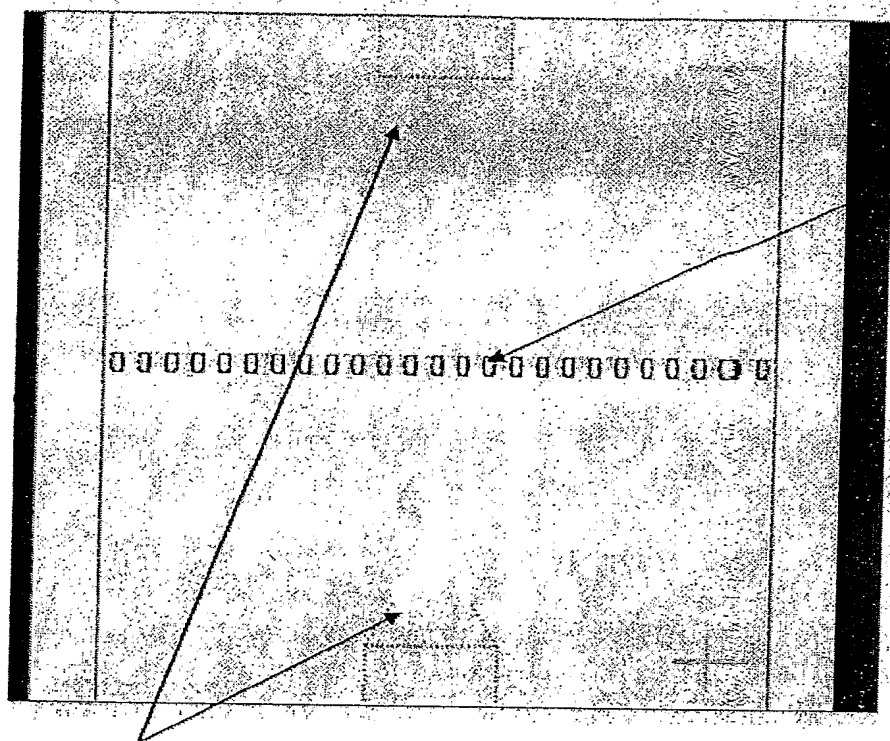


Figure 16

Figure :

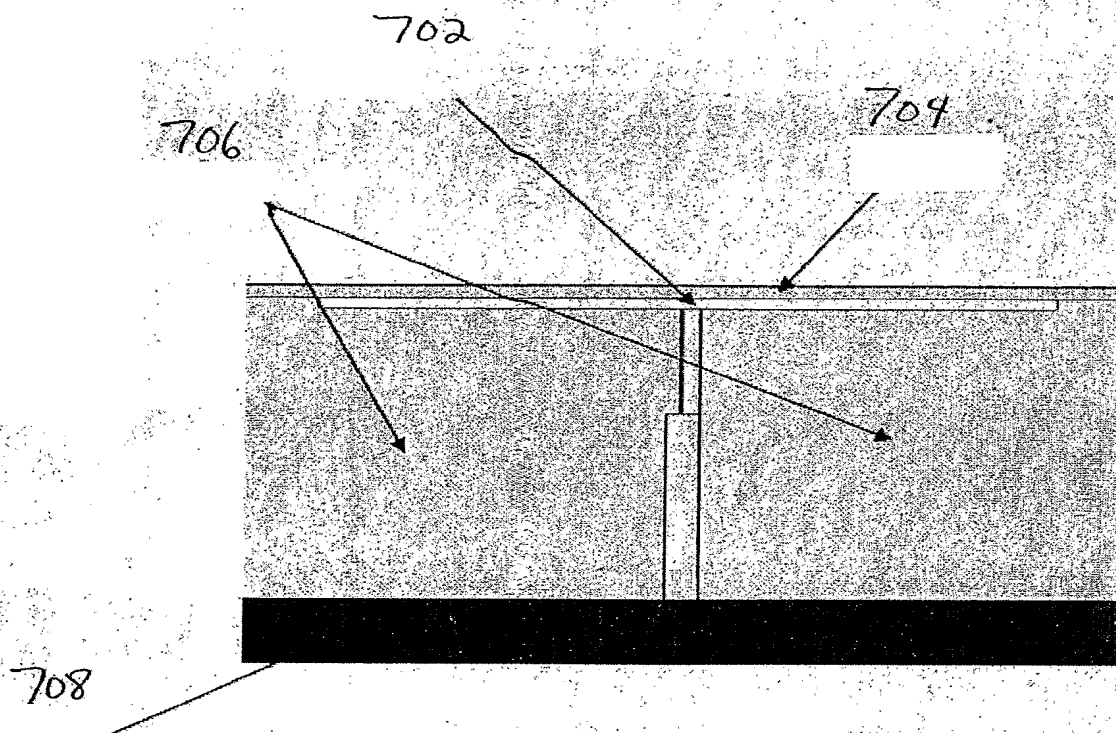
17



702

706

Figure 18





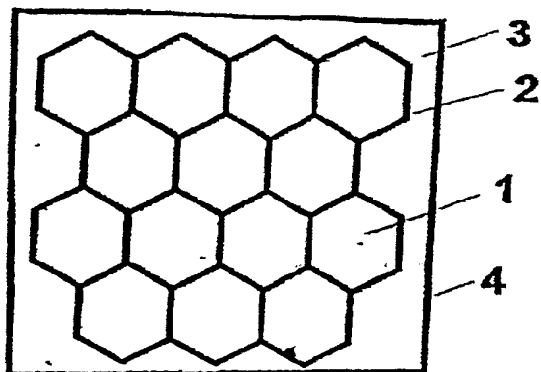


Fig. 19A

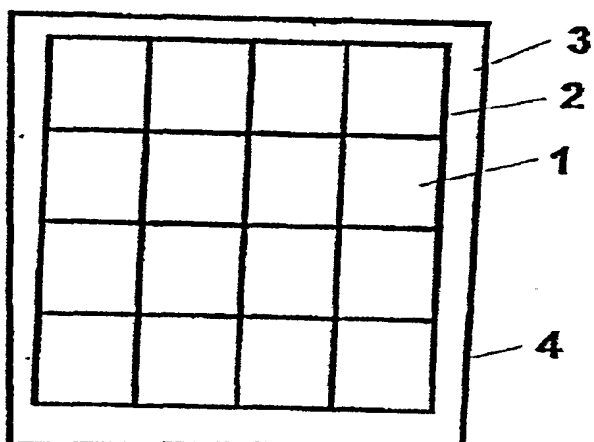


Fig. 19B

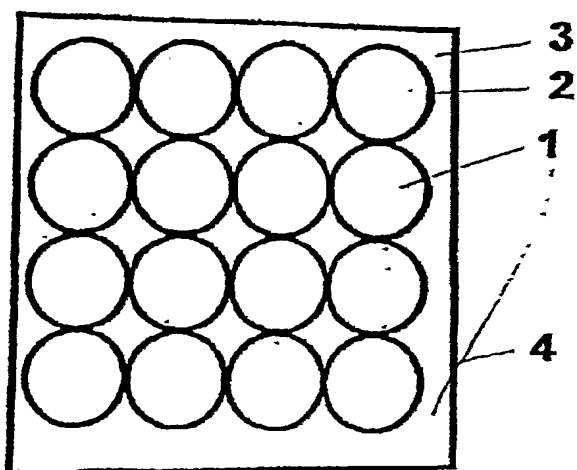
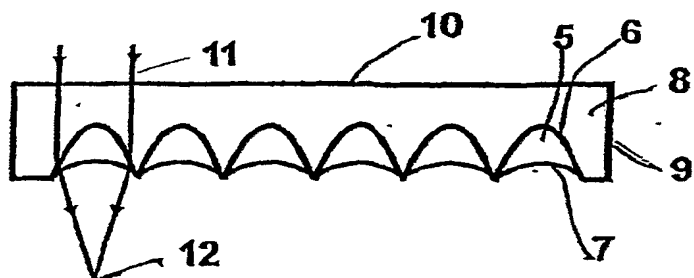
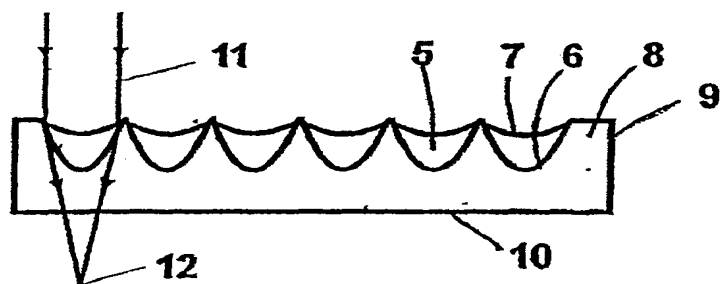


Fig 19C

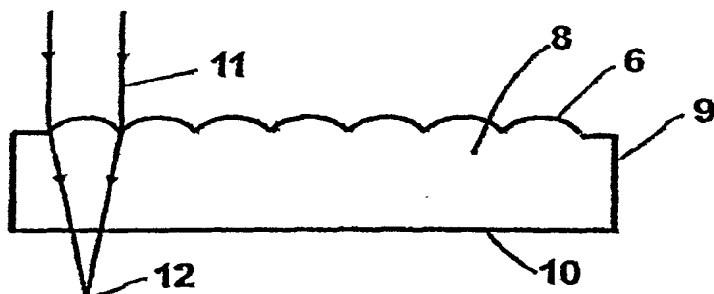


**FIG. 20A**



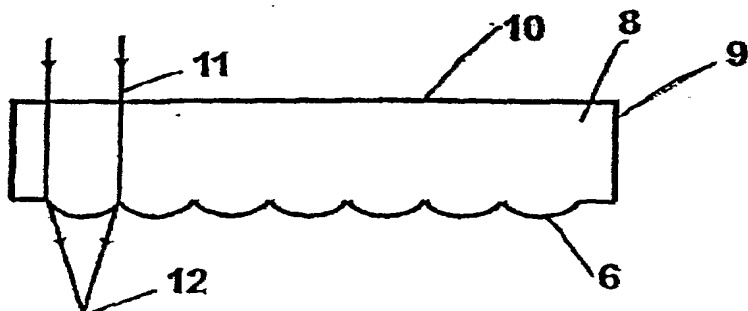
**FIG.**

20B



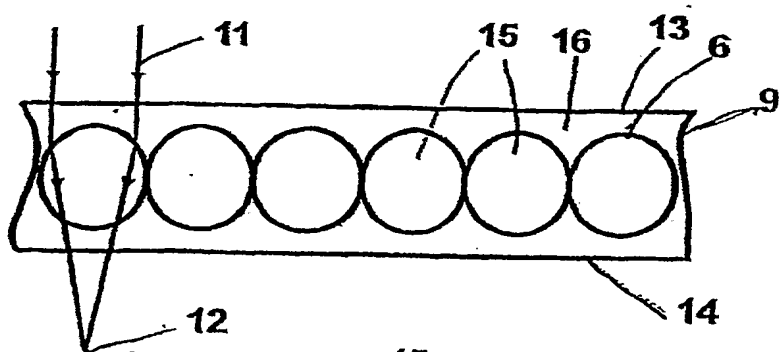
**FIG.**

20C

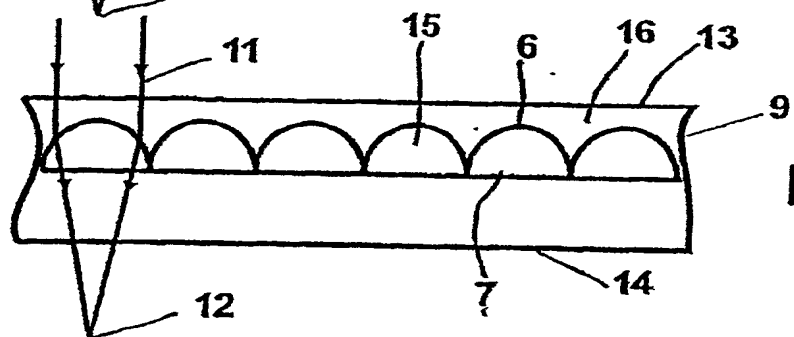


**FIG.**

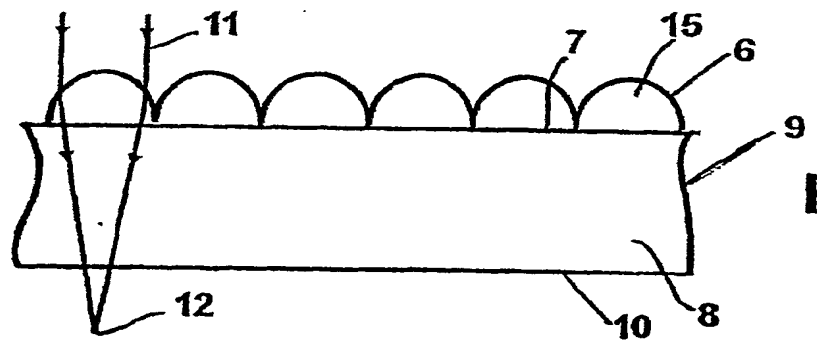
20D



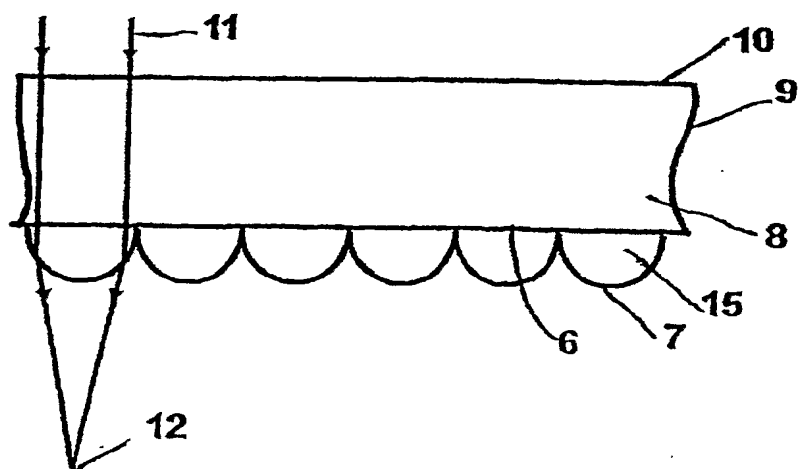
**FIG. 21A**



**FIG. 21B**



**FIG. 21C**



**FIG. 21D**

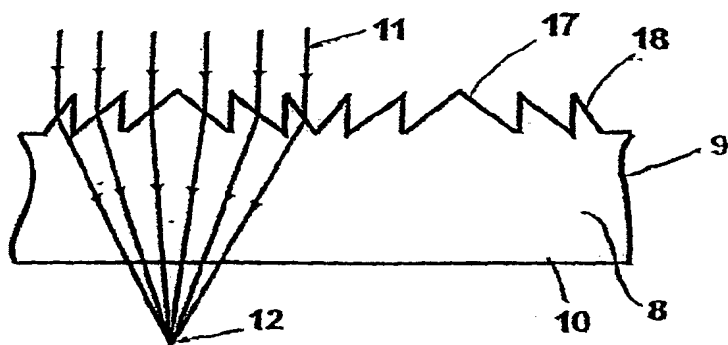


FIG. 22A

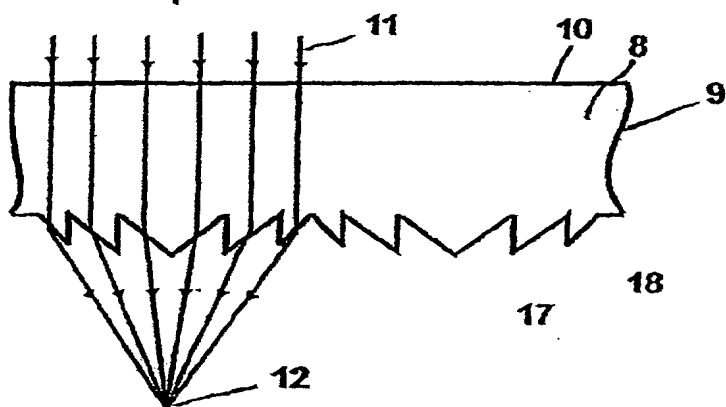


FIG. 22B

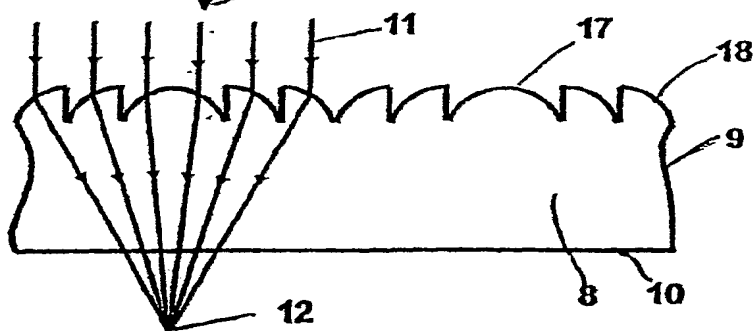


FIG. 22C

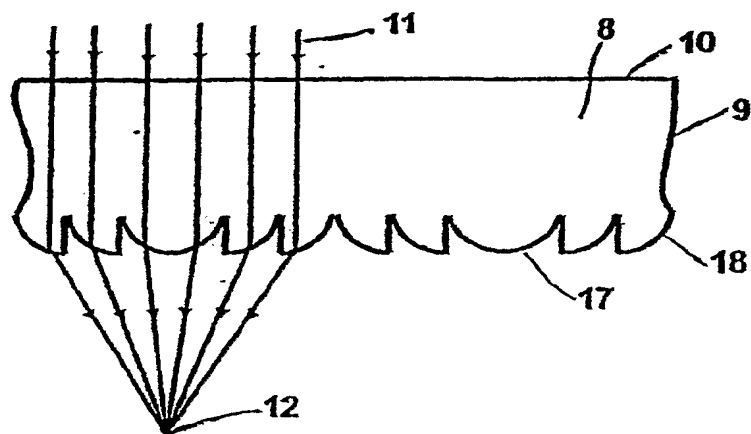


FIG. 22D

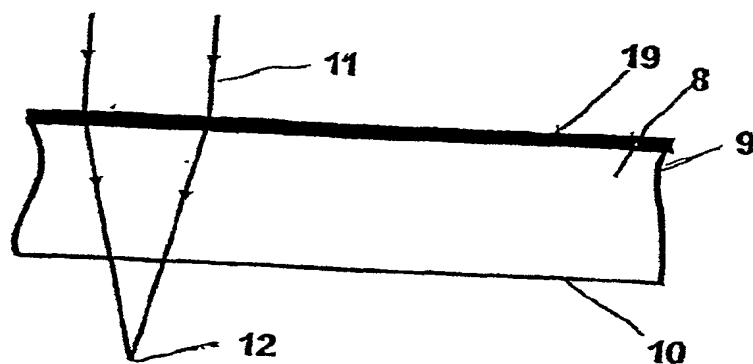


FIG. 23A

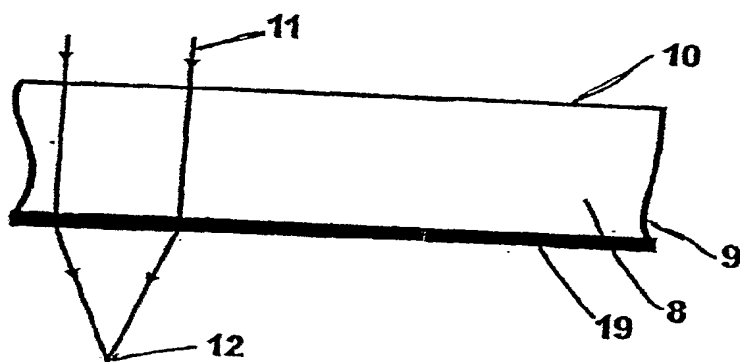


FIG. 23B

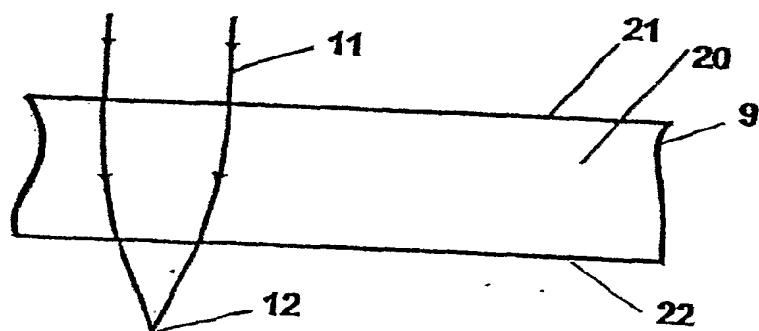


FIG. 23C

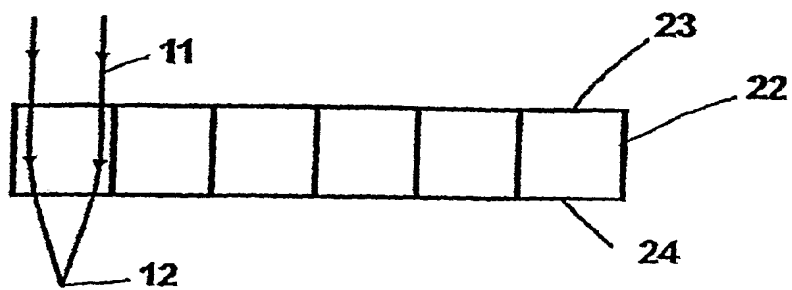


FIG. 24A

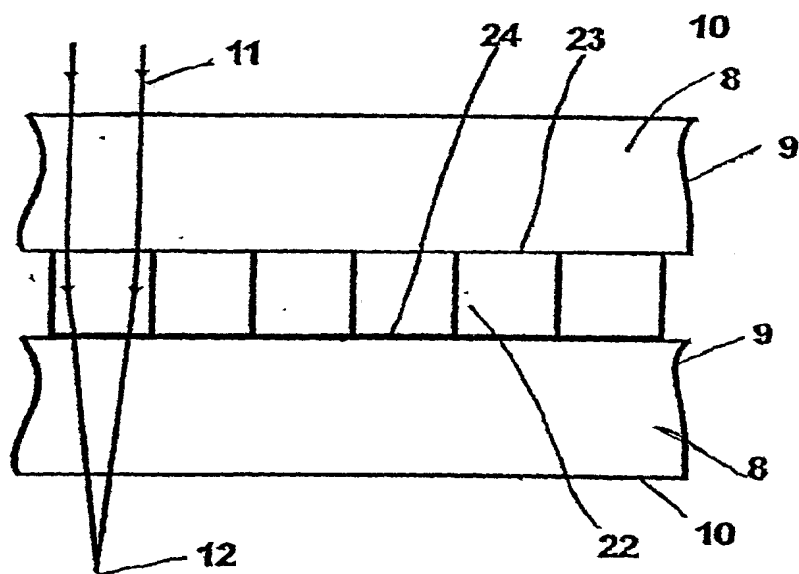


FIG. 24B

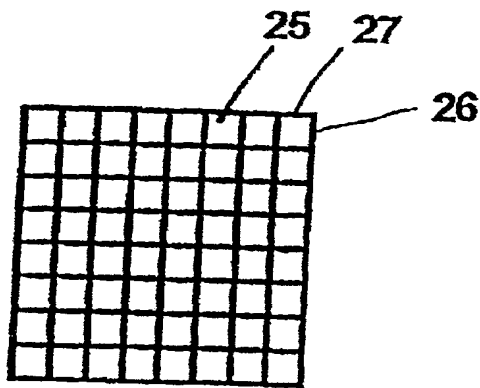


FIG. 25A

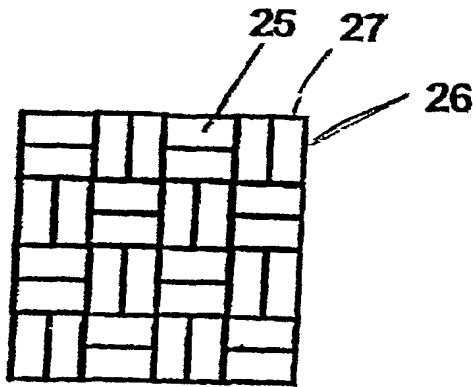


FIG. 25B

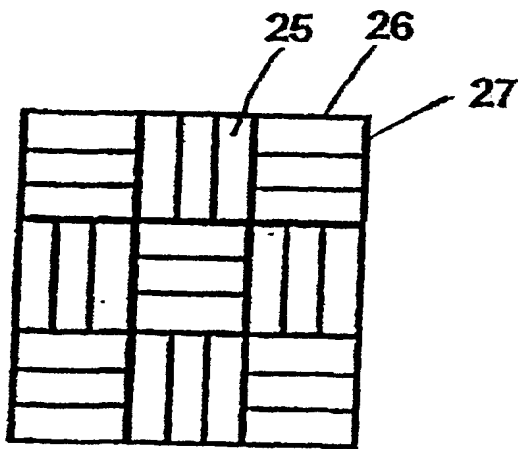
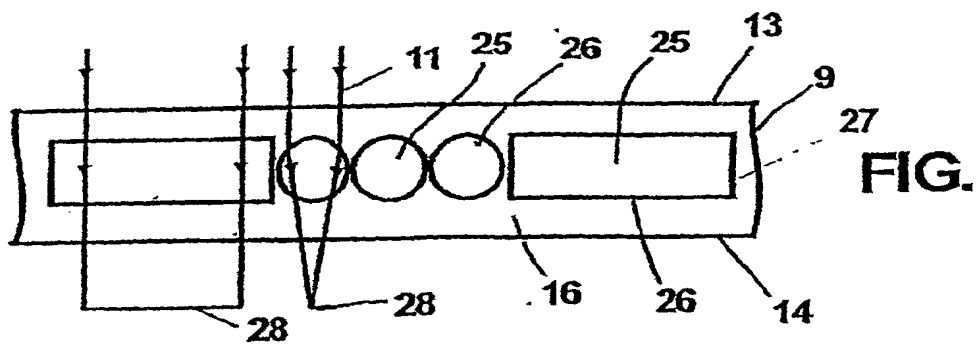
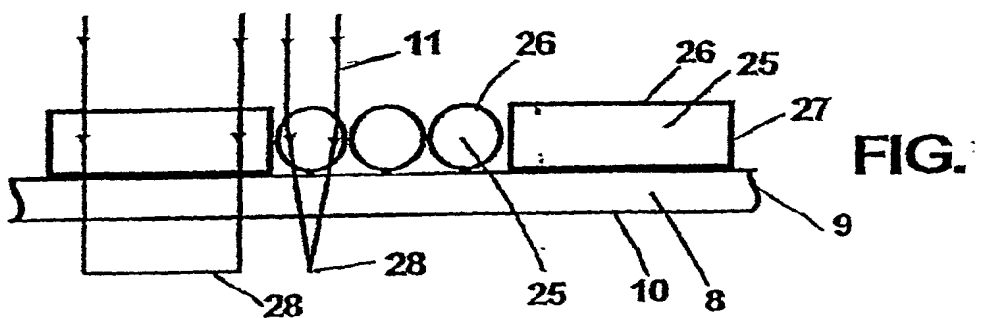


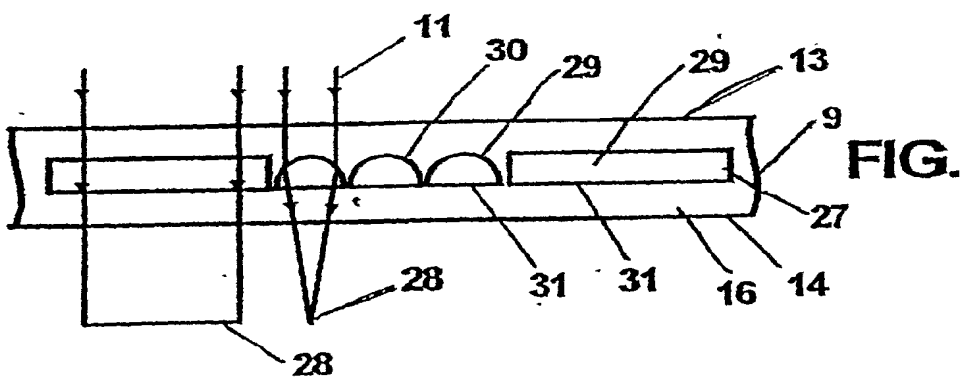
FIG. 25C



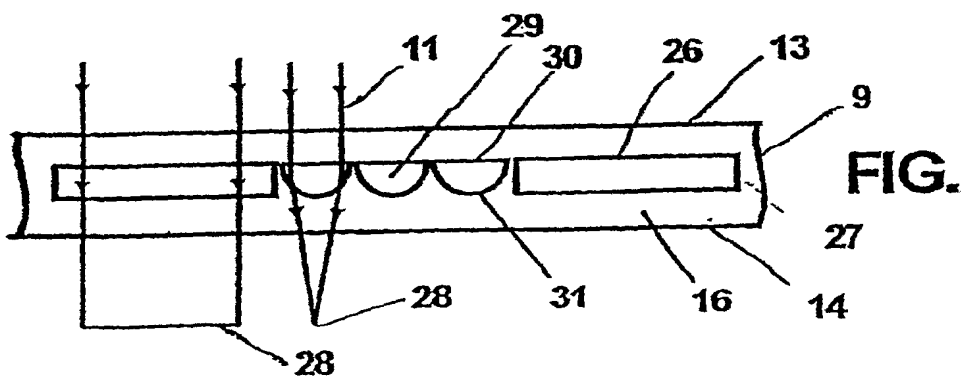
26A



26B



26C



26D



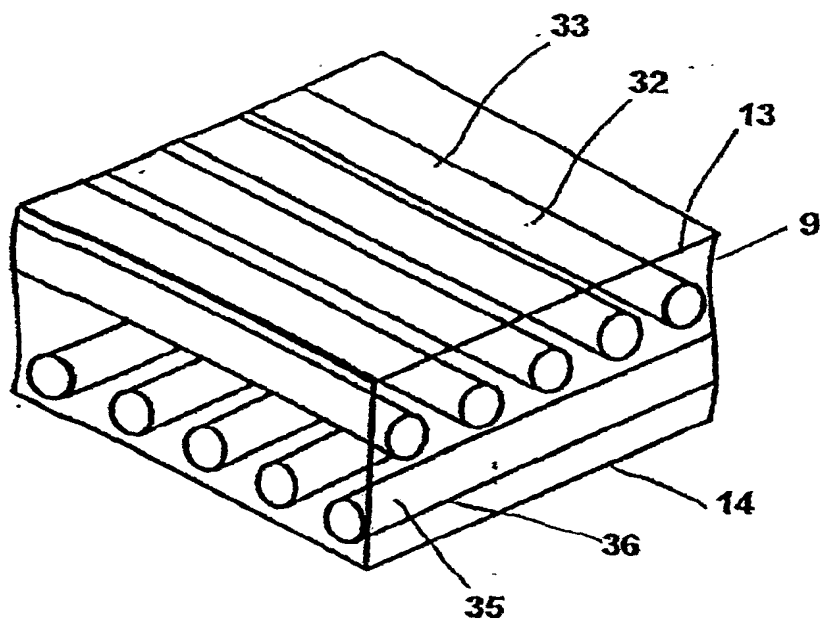


FIG. 27A

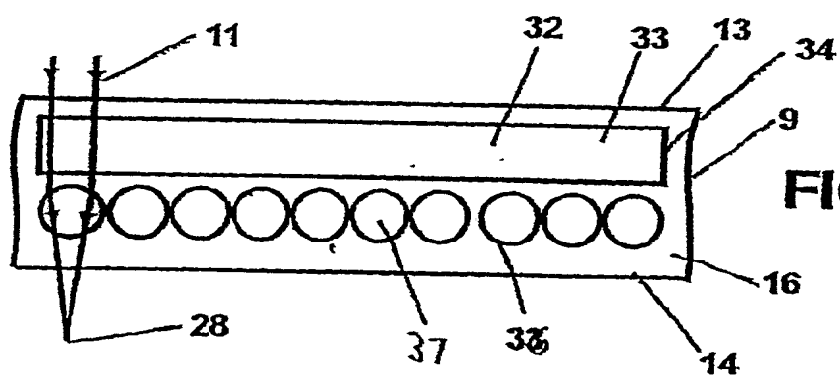


FIG. 27B

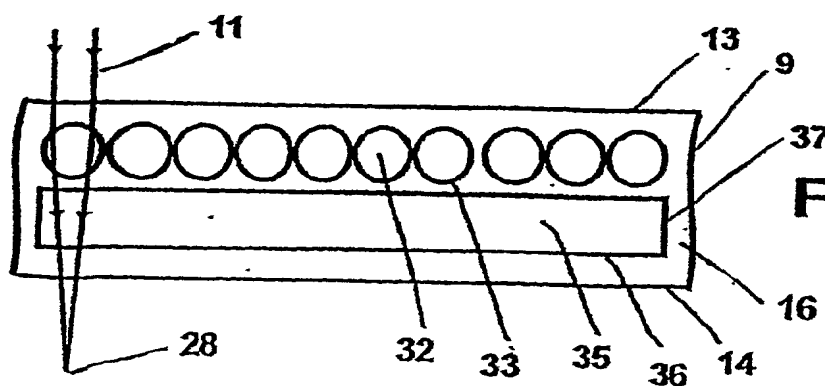


FIG. 27C

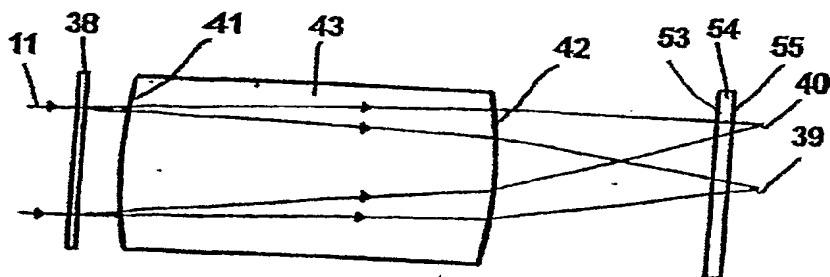


FIG.

28

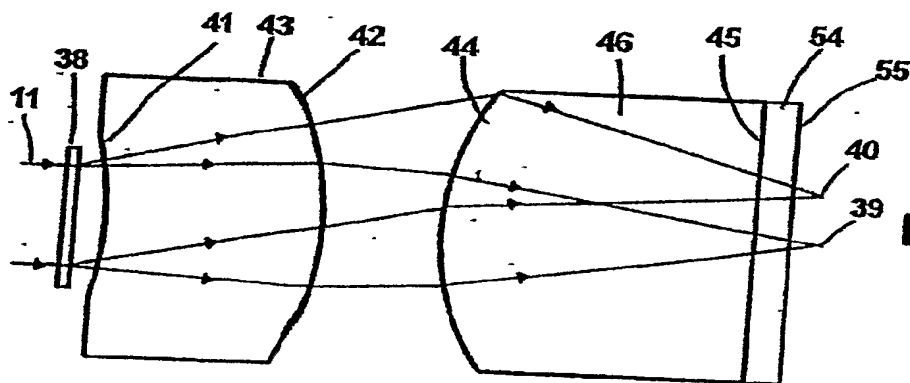


FIG.

29

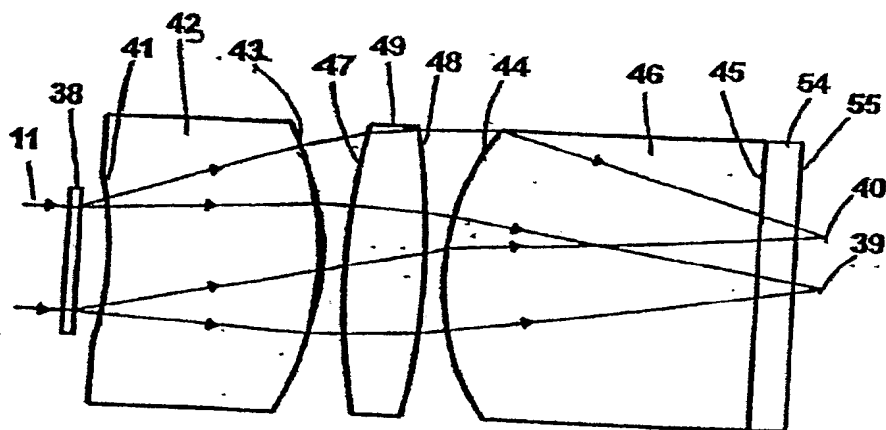


FIG.

30

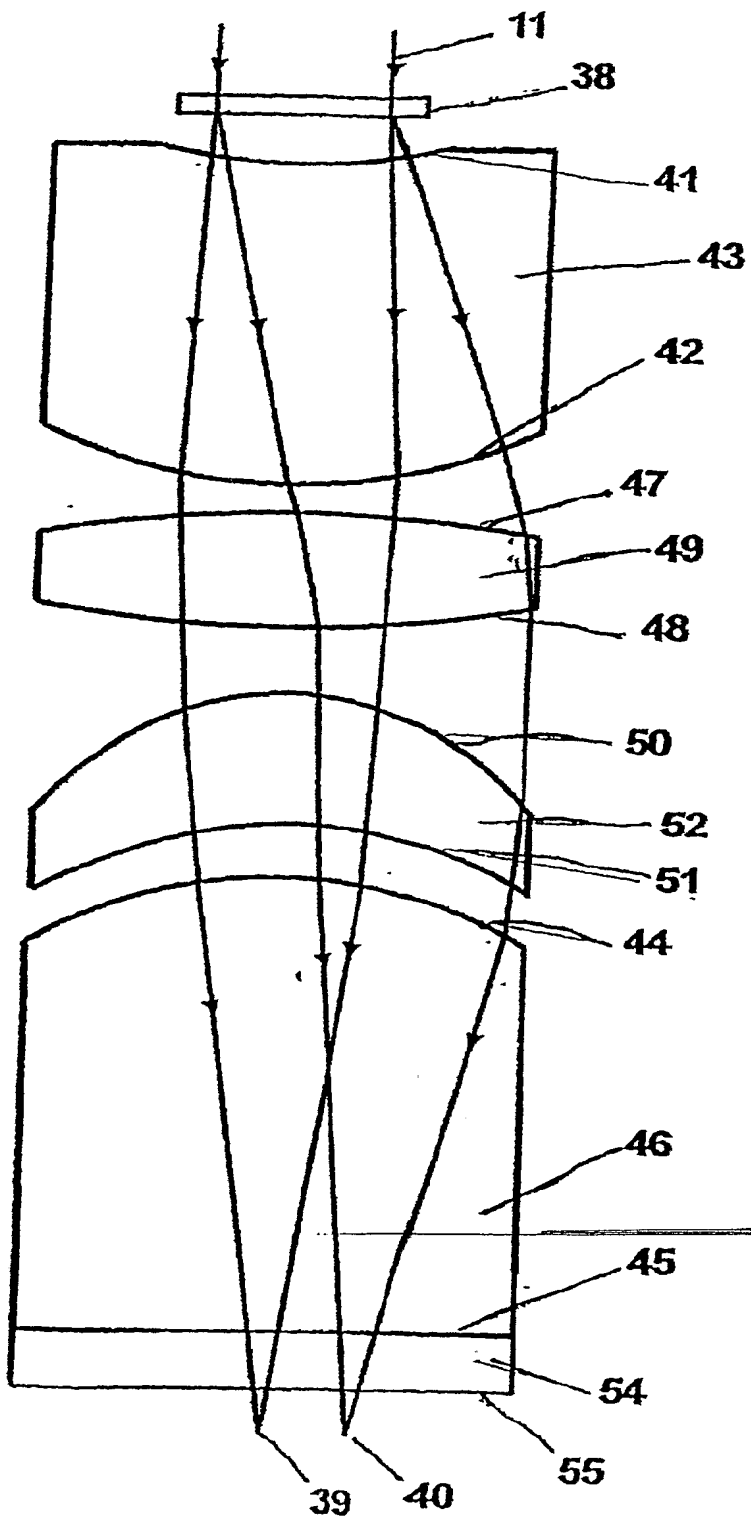


FIG.

31

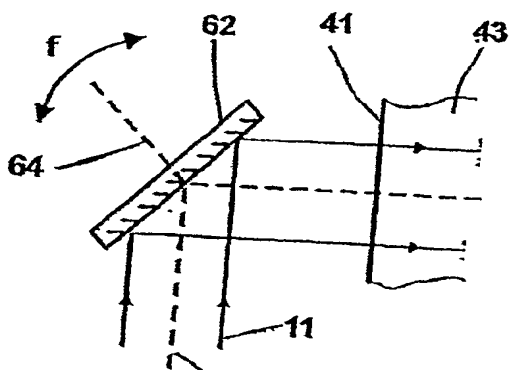


FIG. 32A

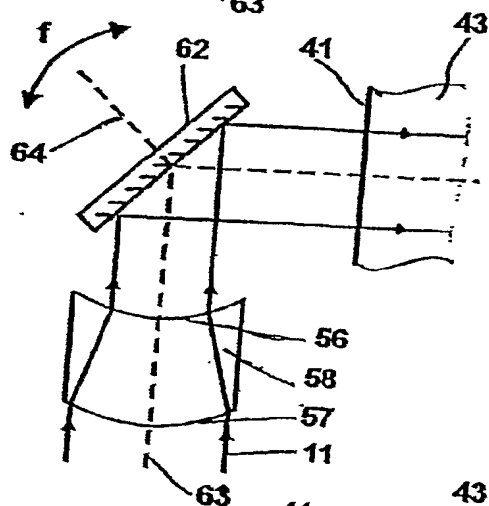


FIG. 32B

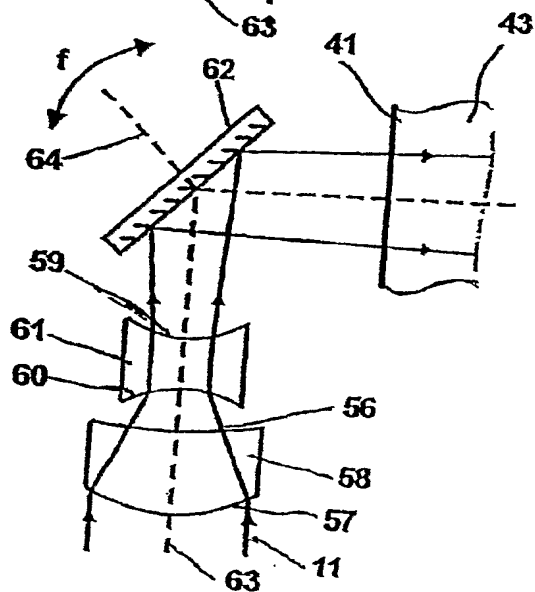


FIG. 32C

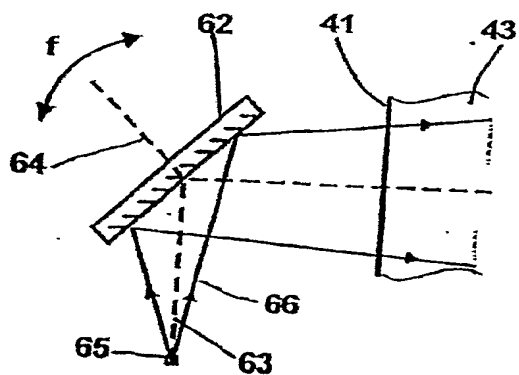


FIG. 33A

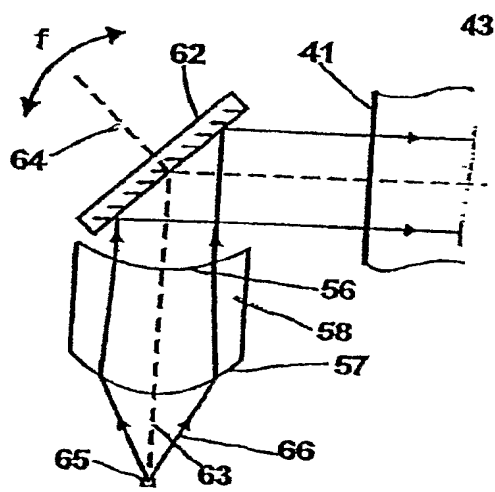


FIG. 33B

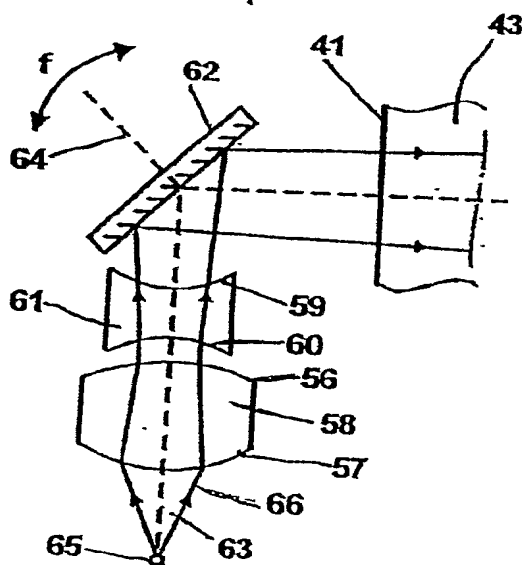


FIG. 33C

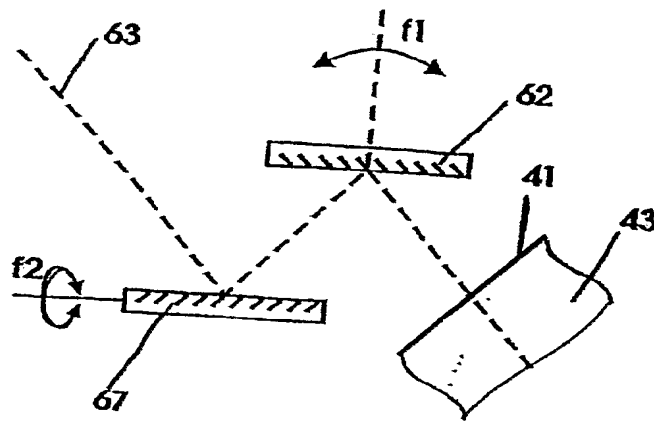


FIG.

34A

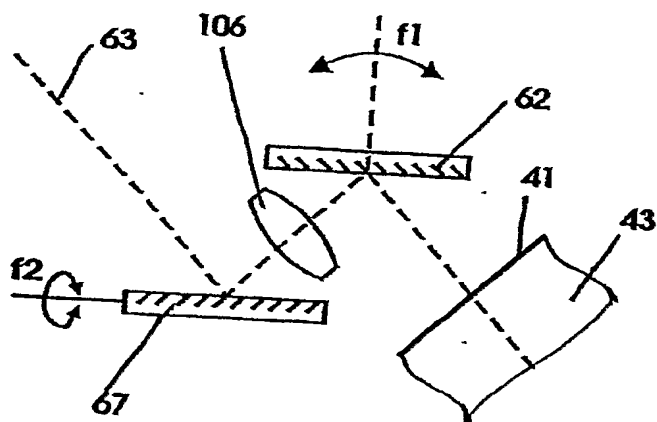


FIG.

34B

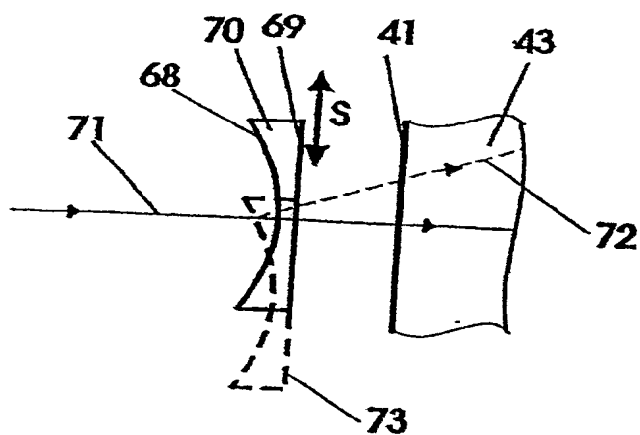


FIG.

35

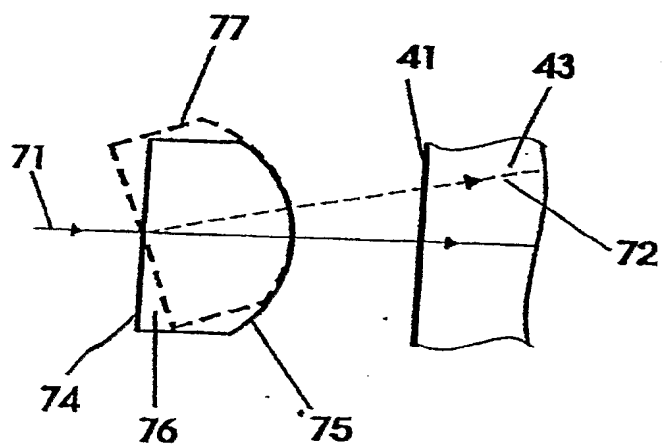


Fig. 36

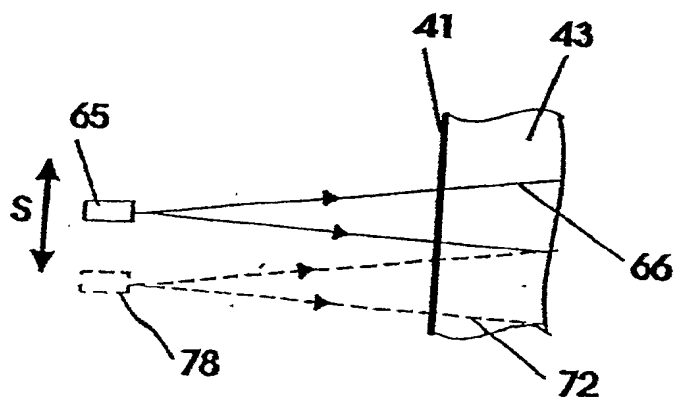
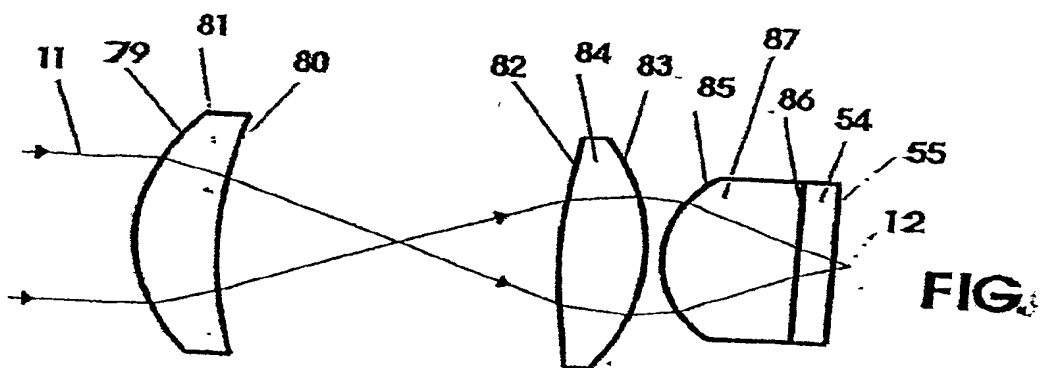


FIG.

37





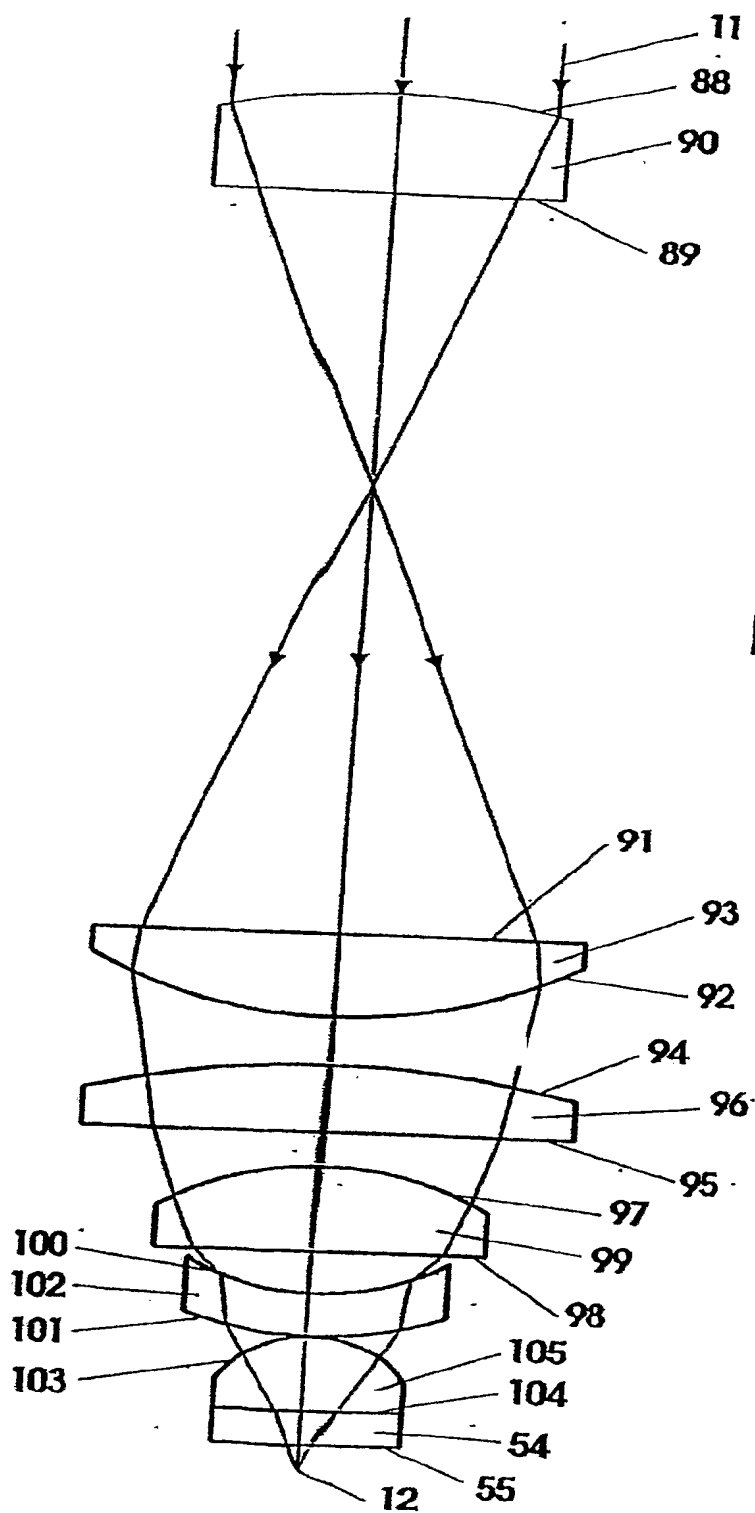
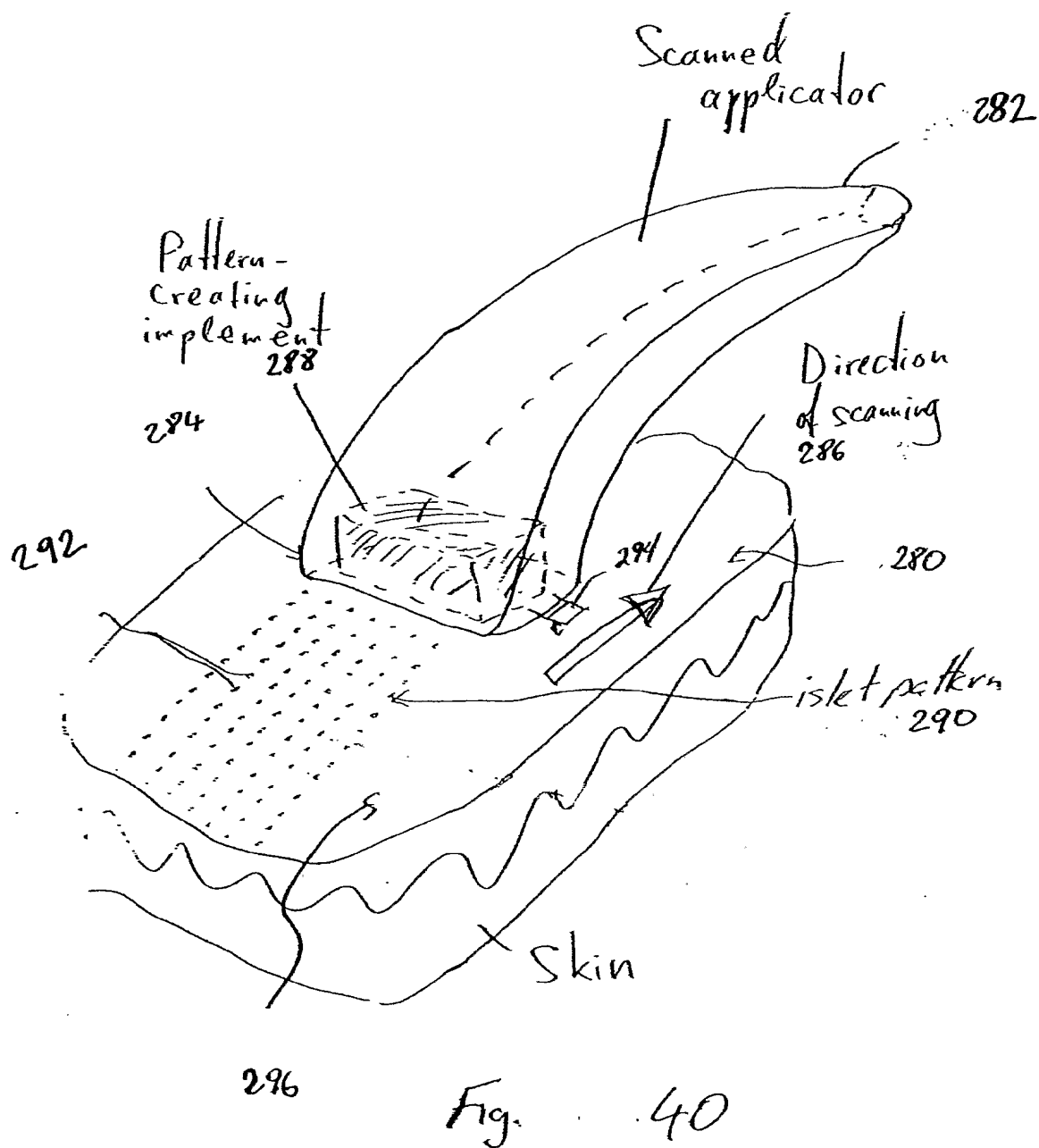


FIG.

39



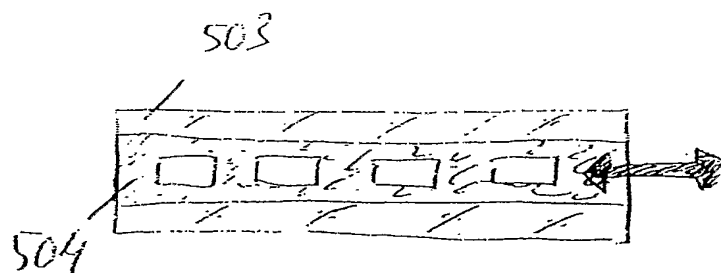
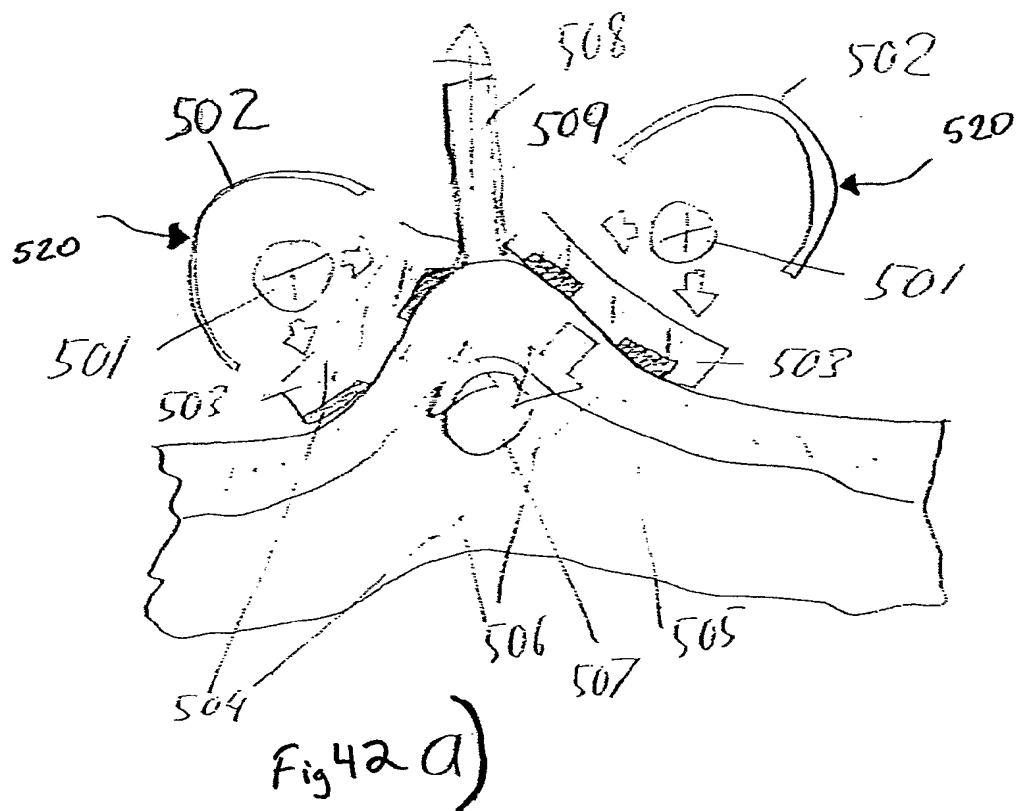


Fig. 42 b)

✓

F42

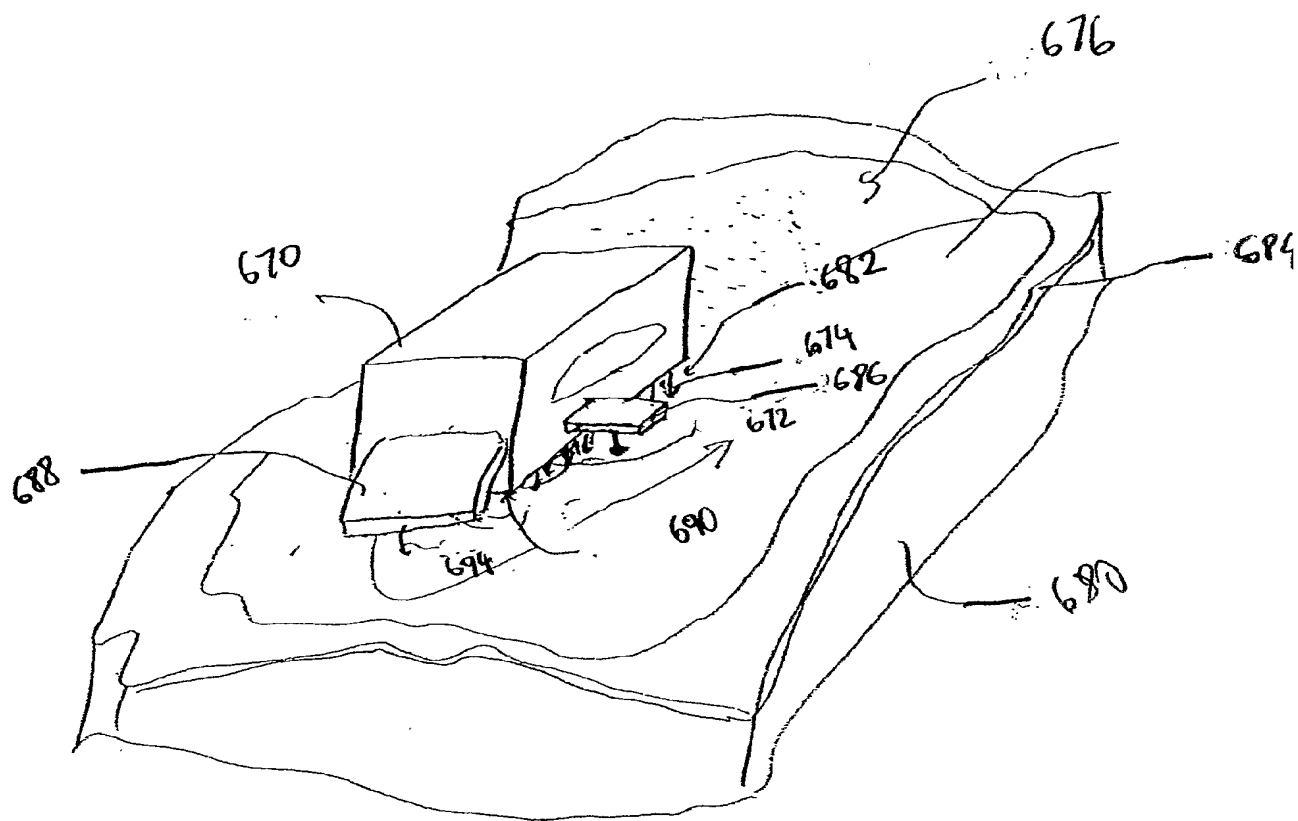


Fig. 44

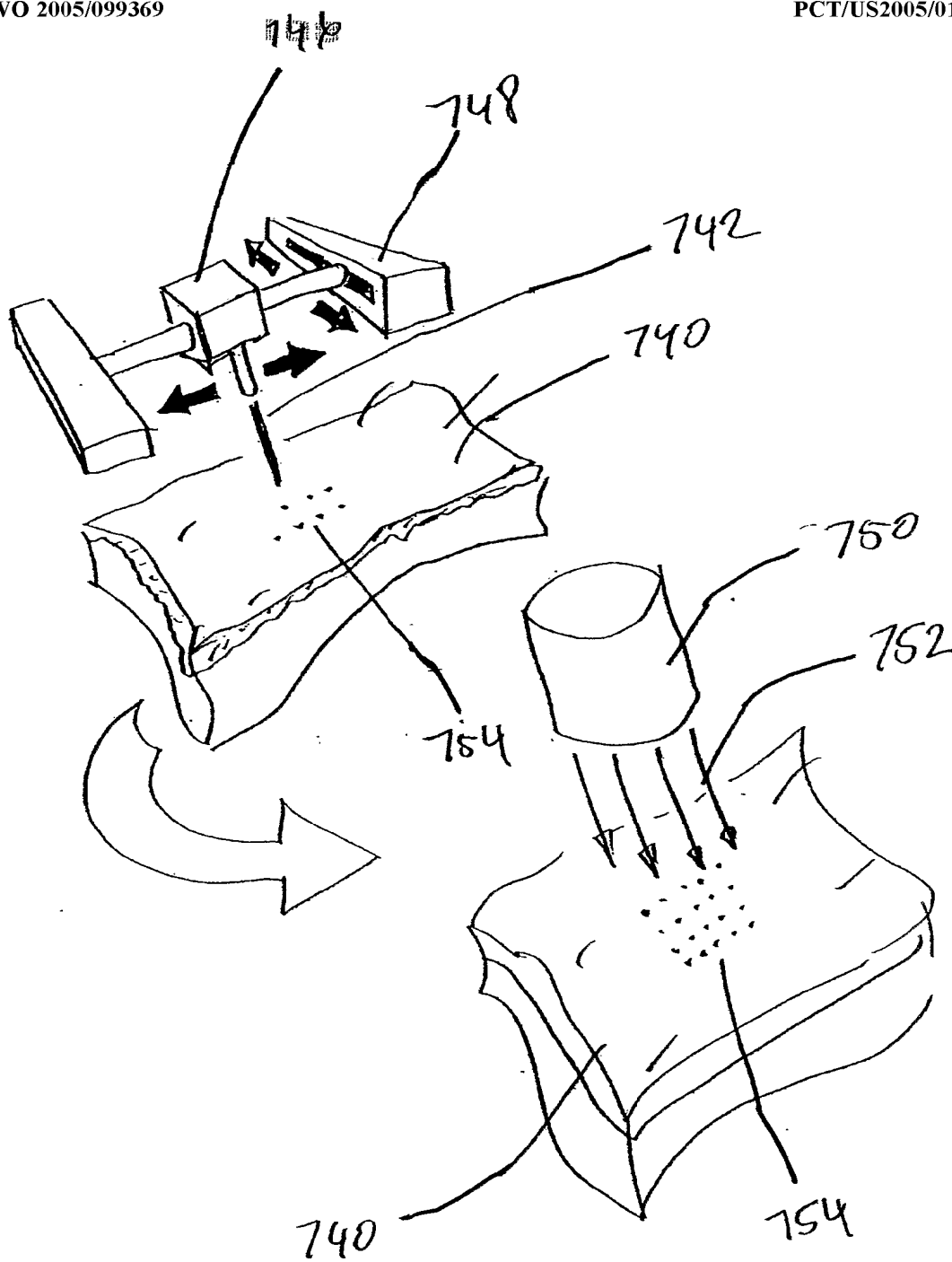


Fig 45

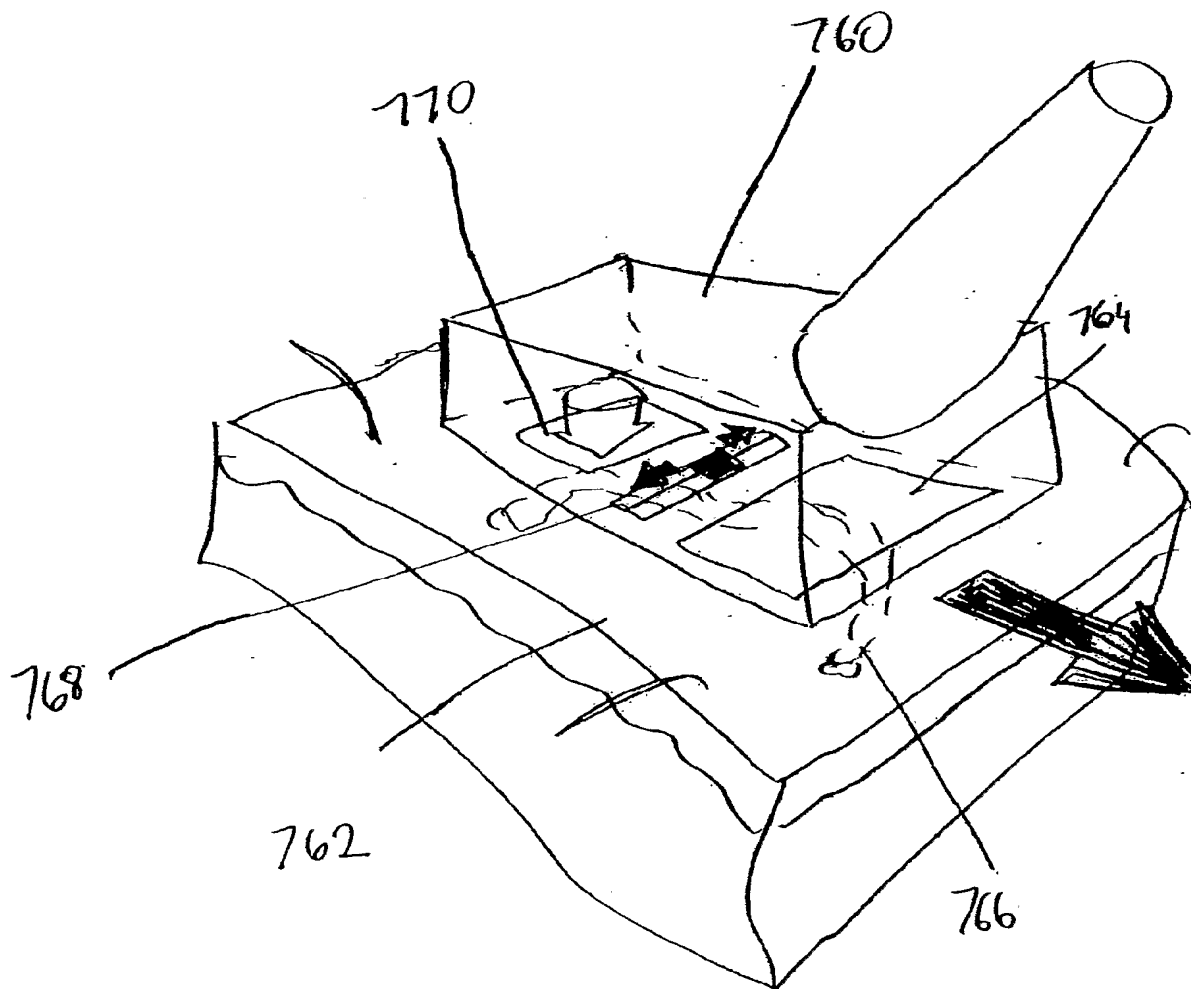


Fig. 46

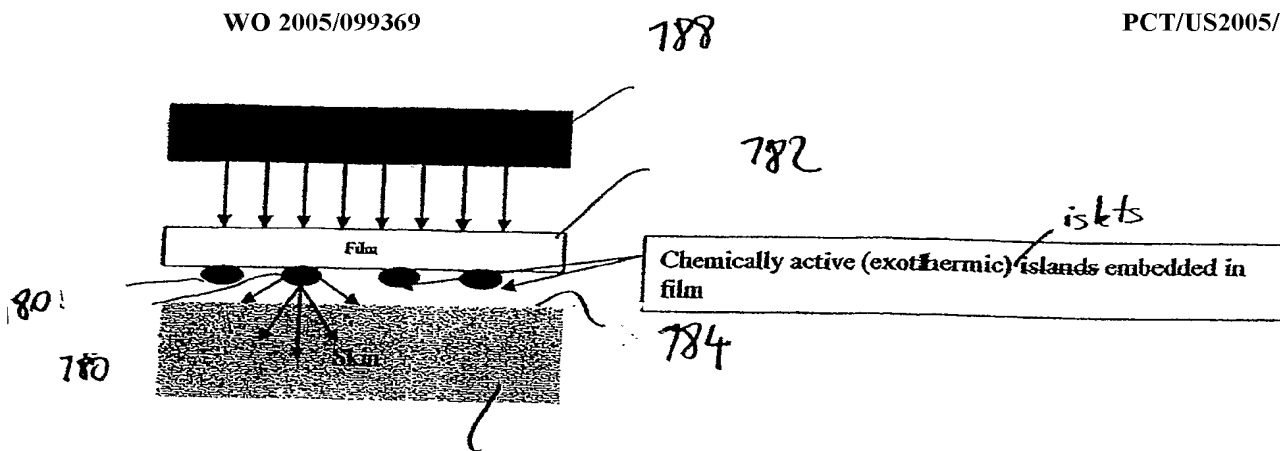


Fig. - 47

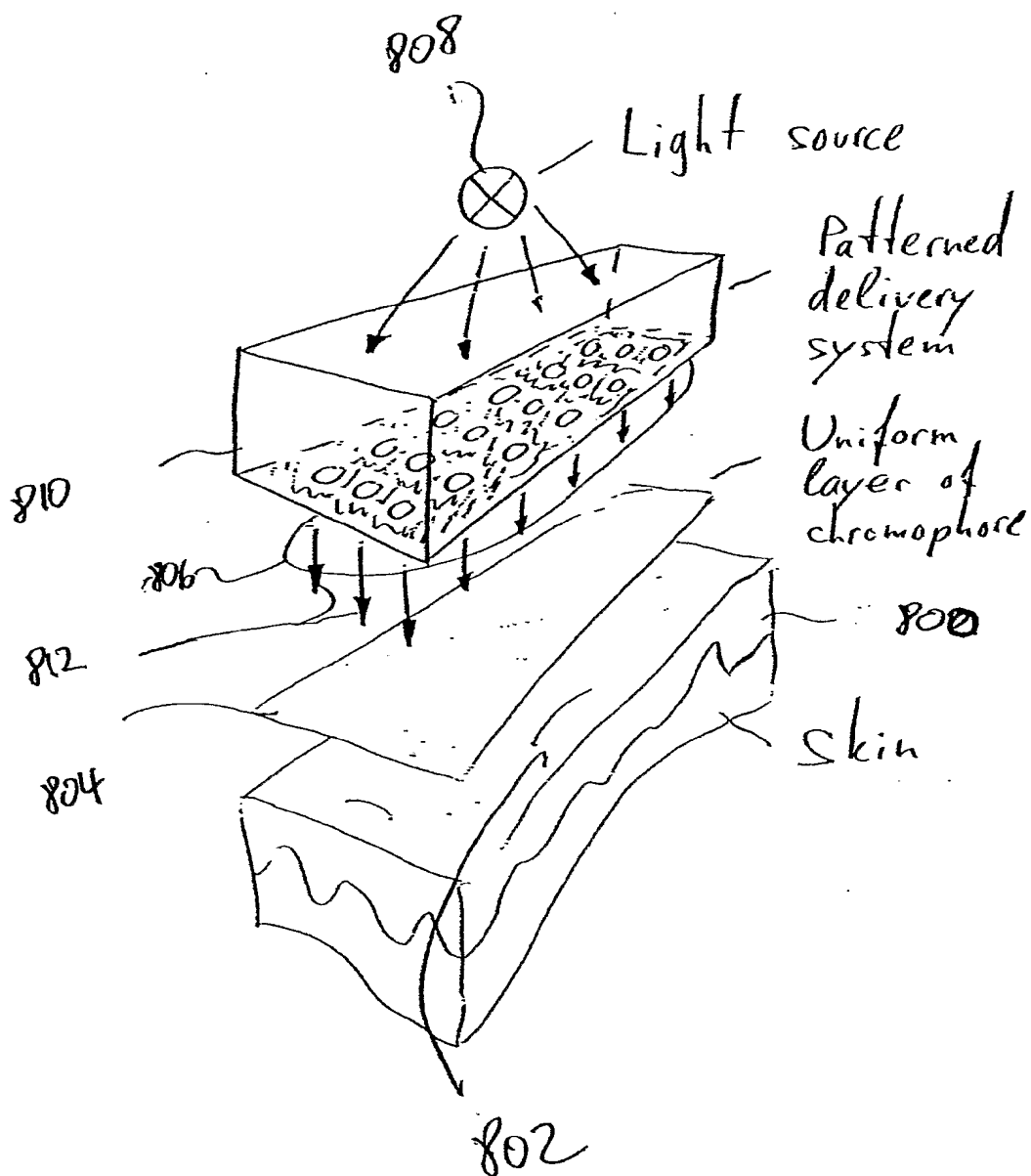


Fig. 48



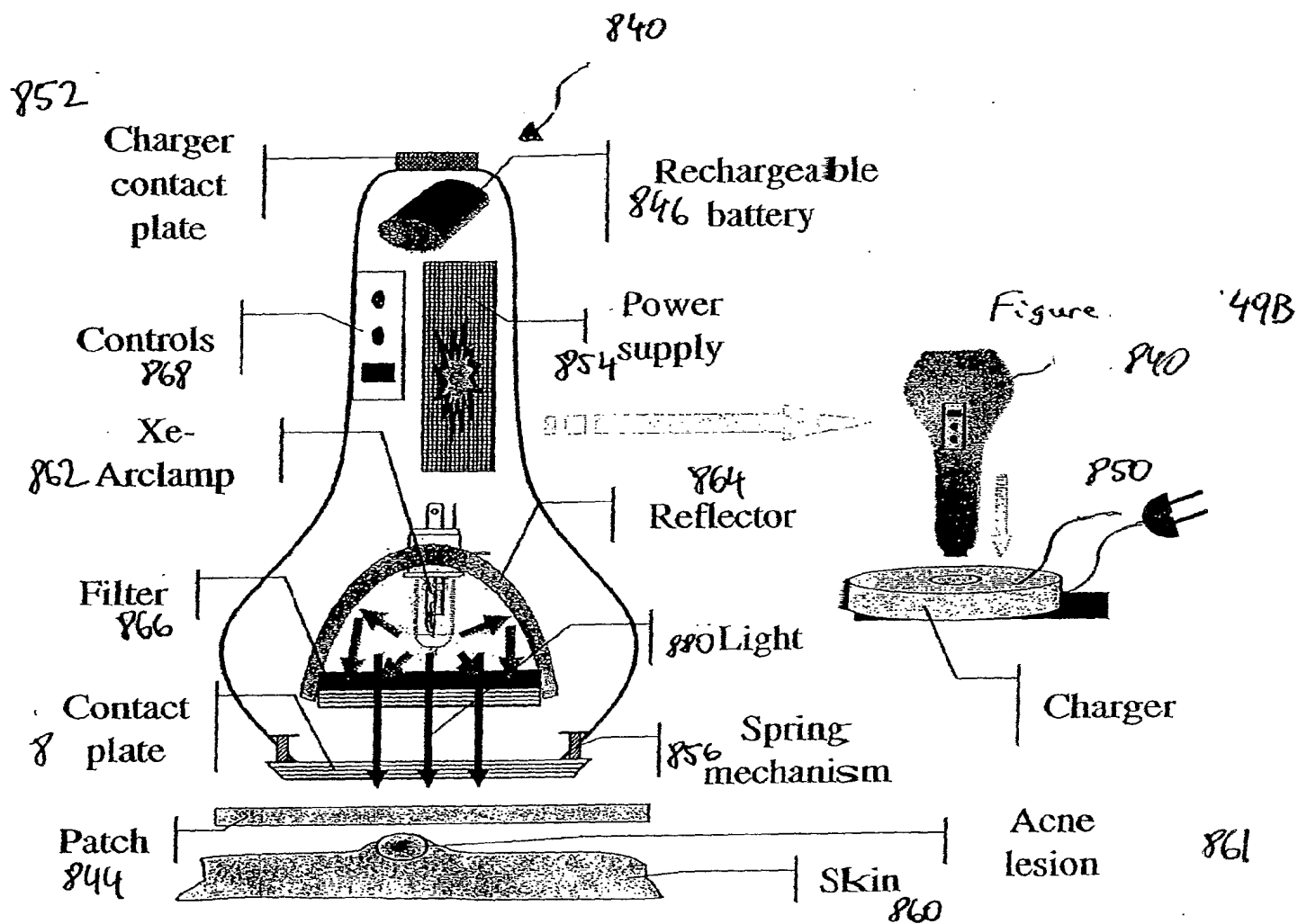


Figure 49A

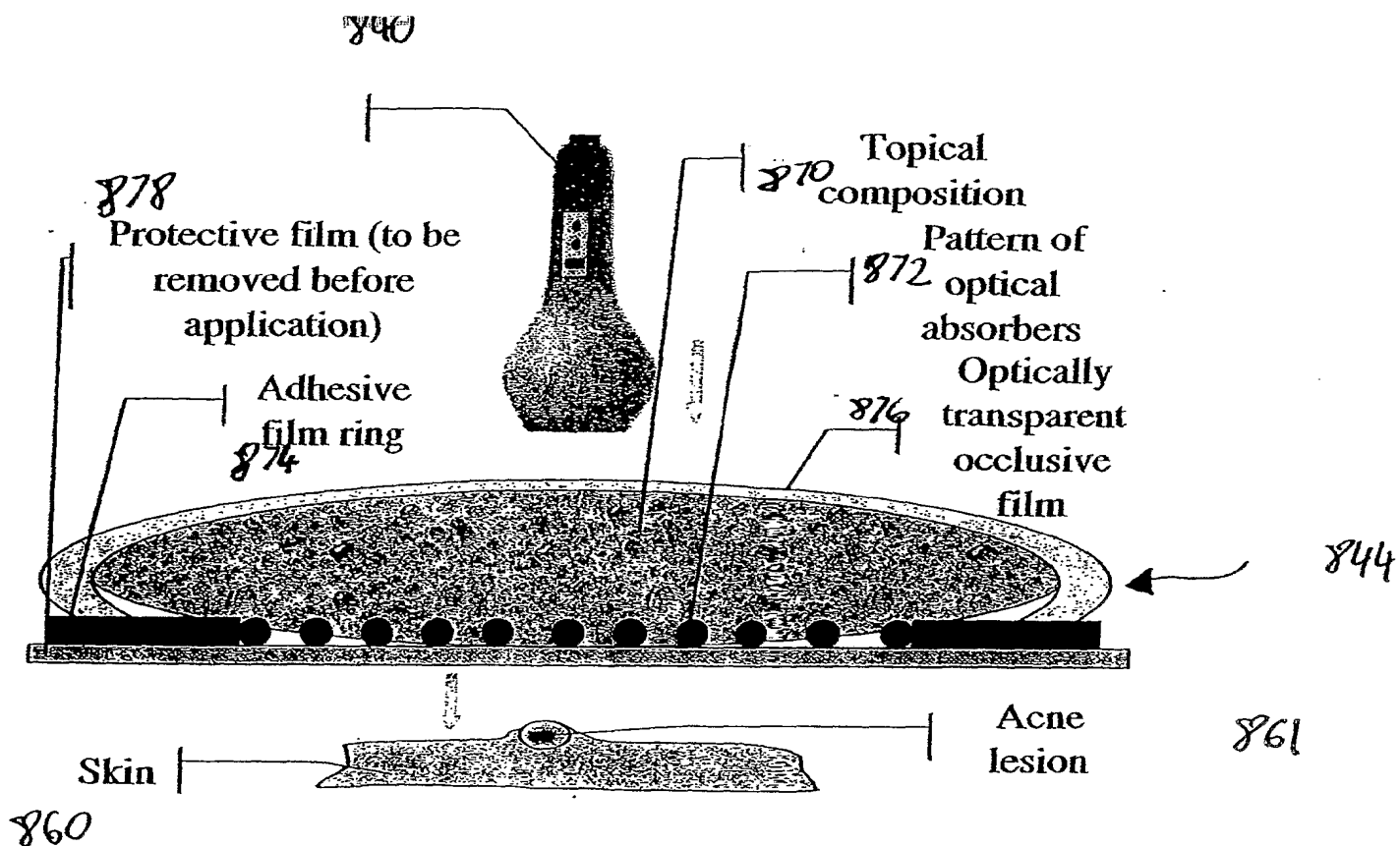
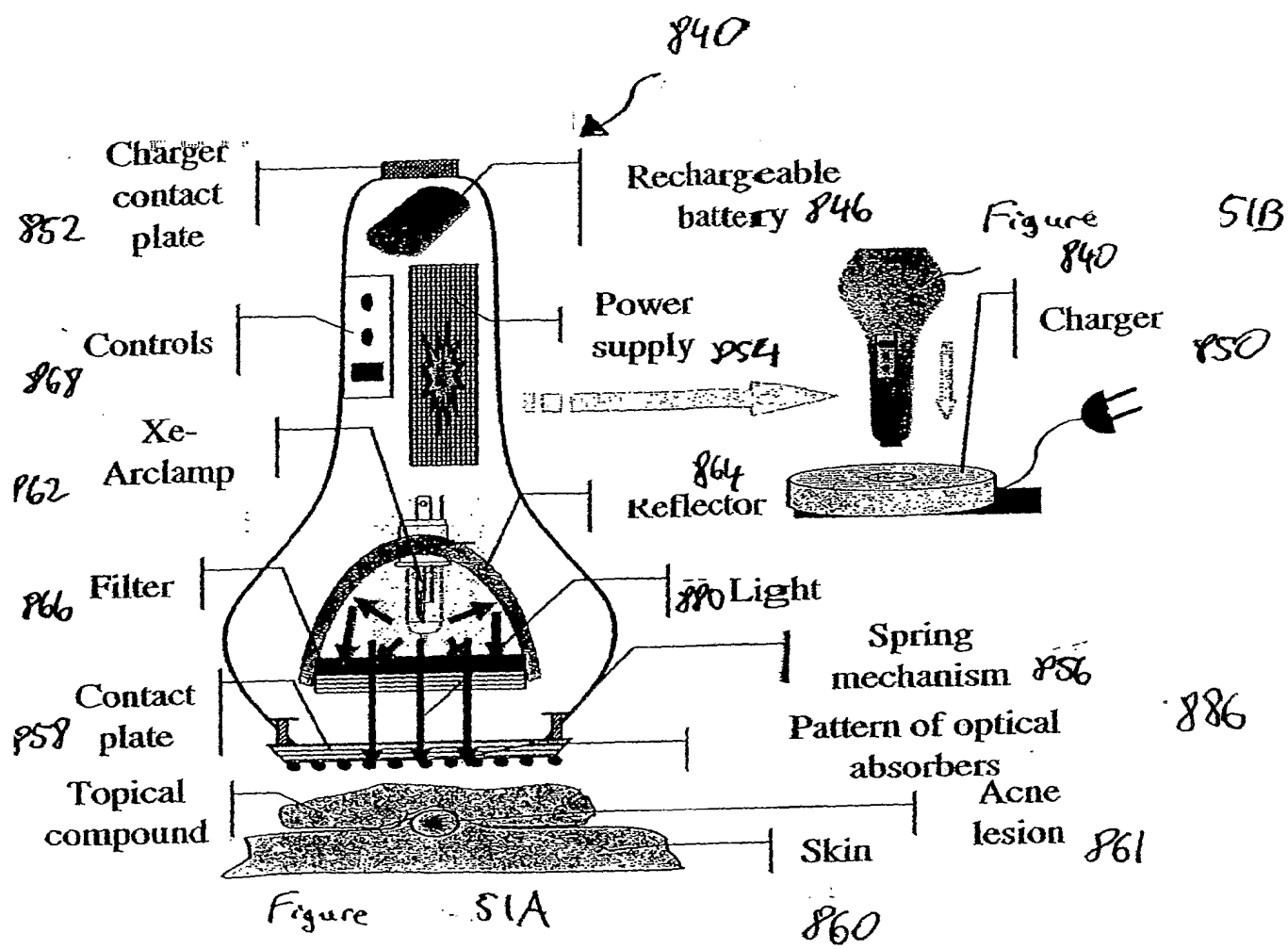
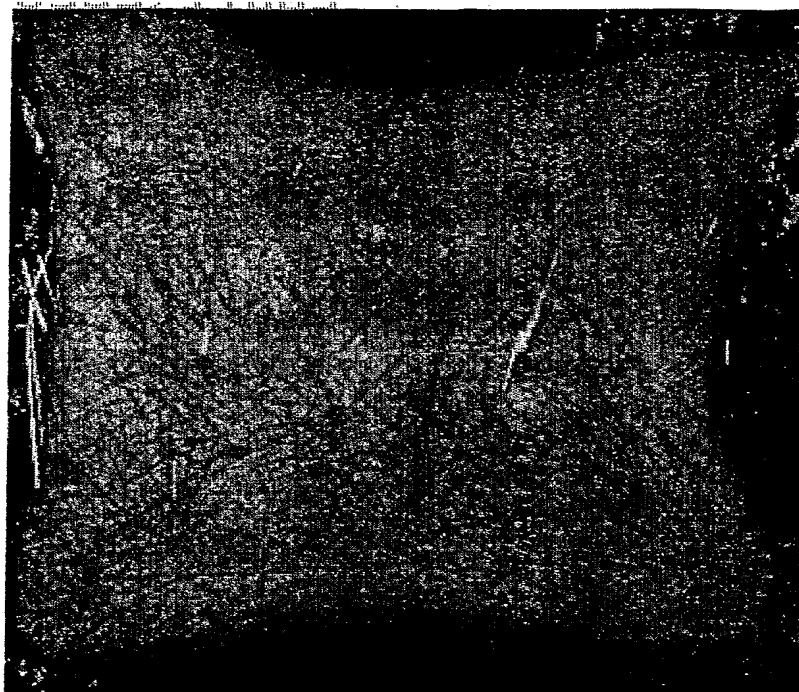


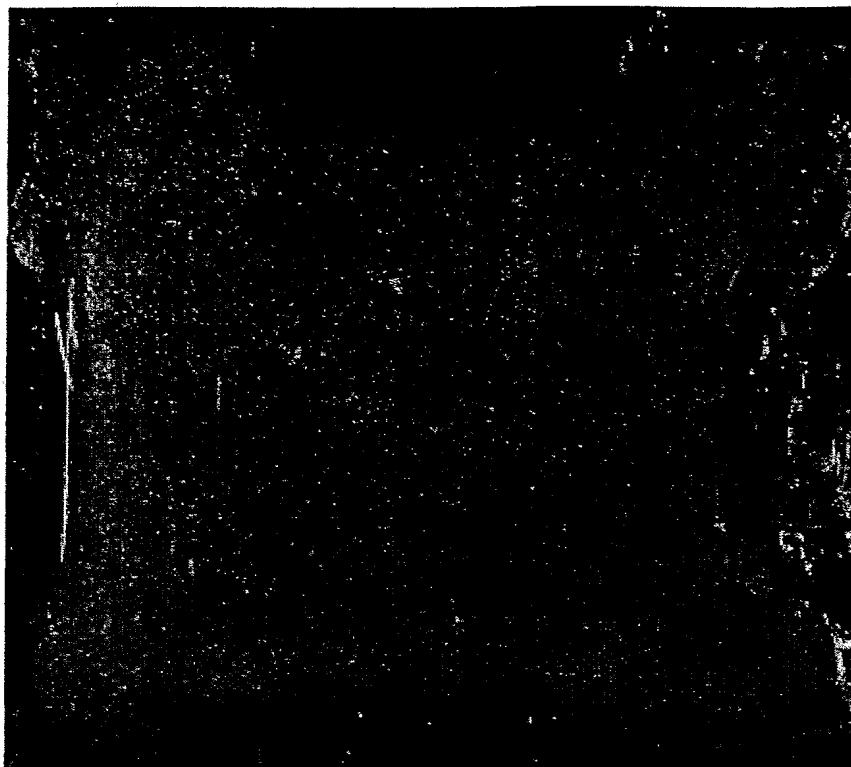
Figure 50





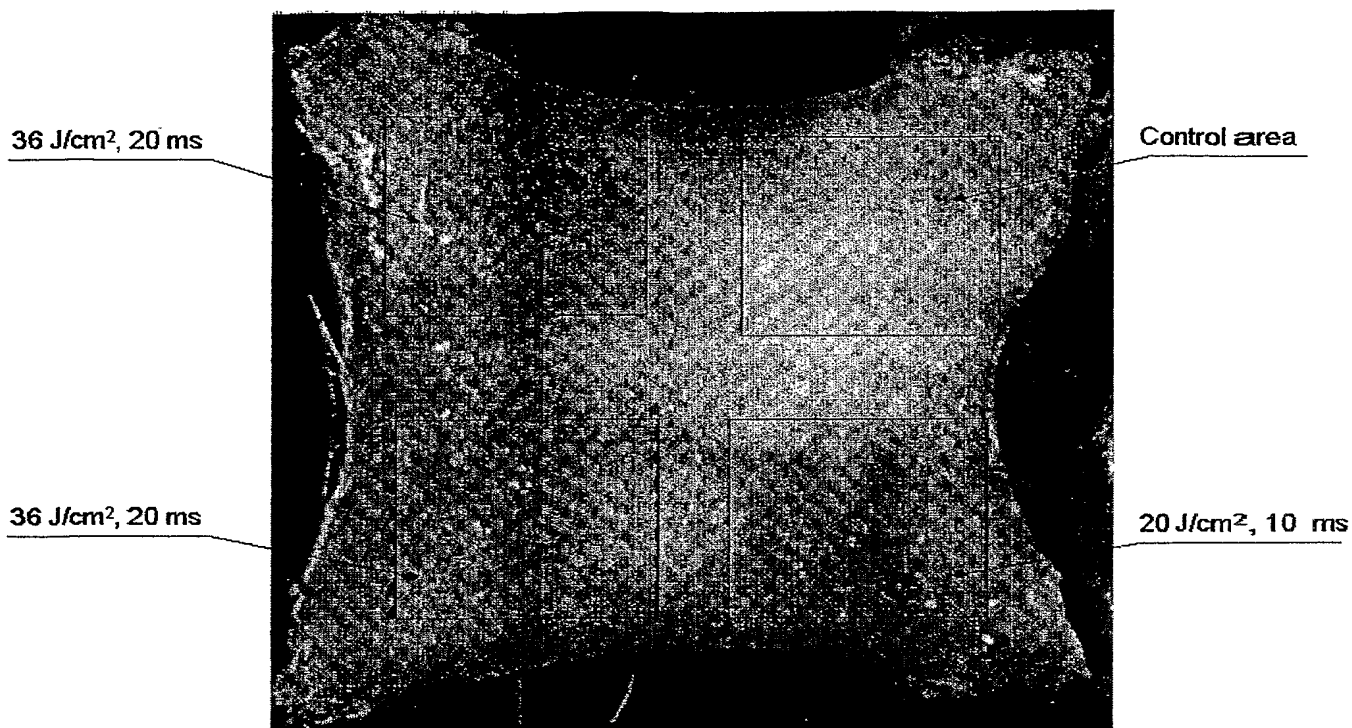
Pre-treatment farm pig skin specimen glued to the rigid transparent substrate.

FIG. 52



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**Figure** Post-treatment farm pig skin specimen glued to the rigid transparent substrate. There are hardly noticeable islands of damage in the stratum corneum of the specimen

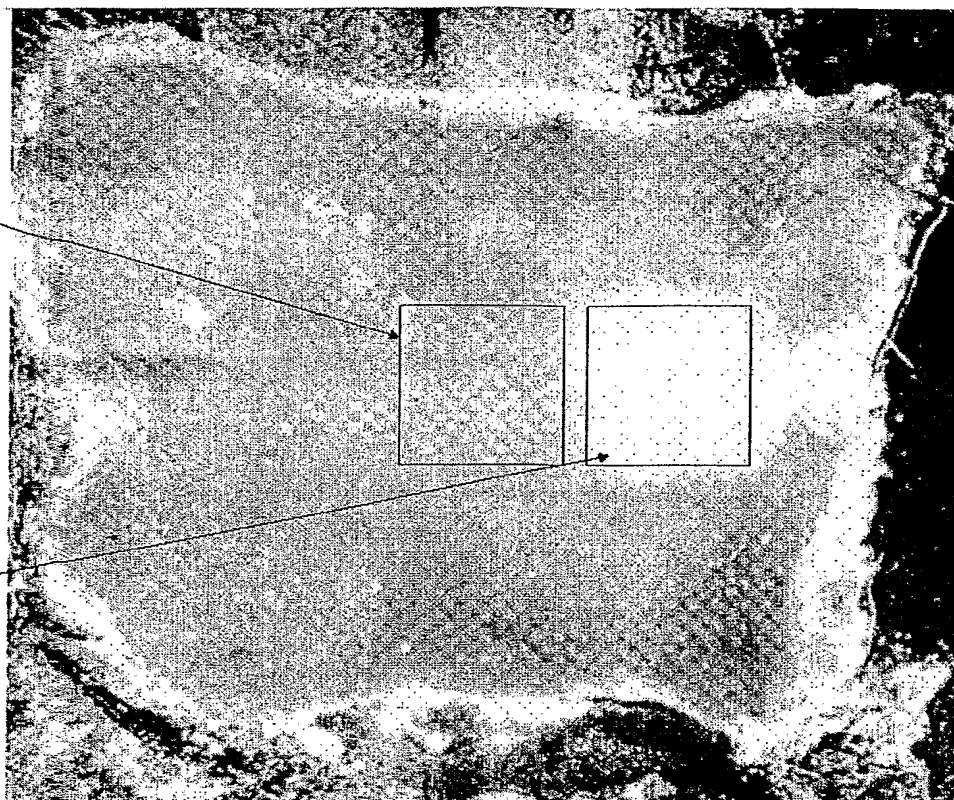


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**Figure 7.** Glucose-treated farm pig skin specimen 60 min after exposure. Maximum optical clearance was observed for 36 J/cm<sup>2</sup> fluence, 20 ms pulse. No detectable clearance was observed at the control (non-treated) area.

One pulse of  $36\text{ J/cm}^2 - 20\text{ ms}$

One pulse of  $36\text{ J/cm}^2 - 20\text{ ms}$   
plus two pulse of  $36\text{ J/cm}^2 - 20\text{ ms}$   
one hour late



55

Figure 55 Glucose-treated farm pig skin specimen 3 hrs. after exposure. Picture is taken in transillumination mode, with the specimen backlit by a CW lamp. Specimen area treated with three pulses of  $36\text{ J/cm}^2 / 20\text{ ms}$  shows total optical clearance. Specimen area treated with one pulse of  $36\text{ J/cm}^2 / 20\text{ ms}$  shows only partial optical clearance.

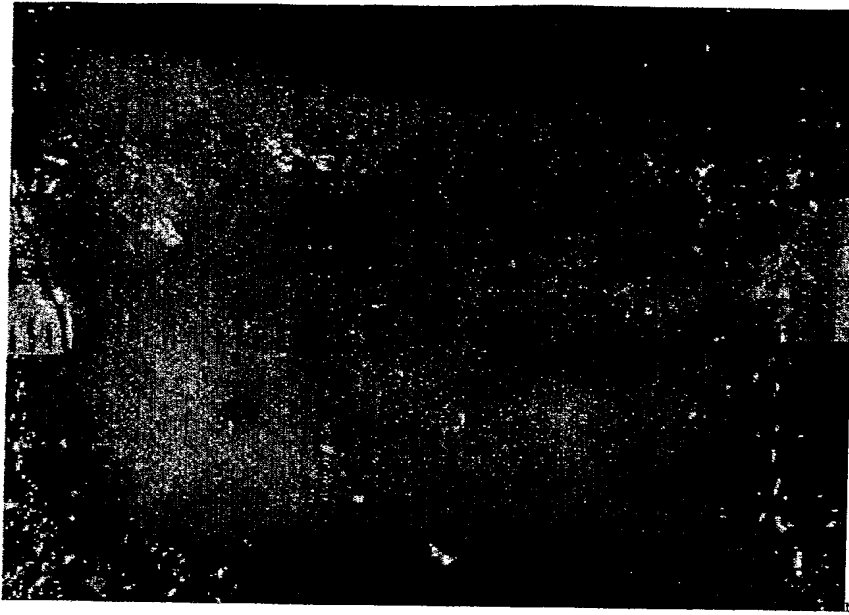
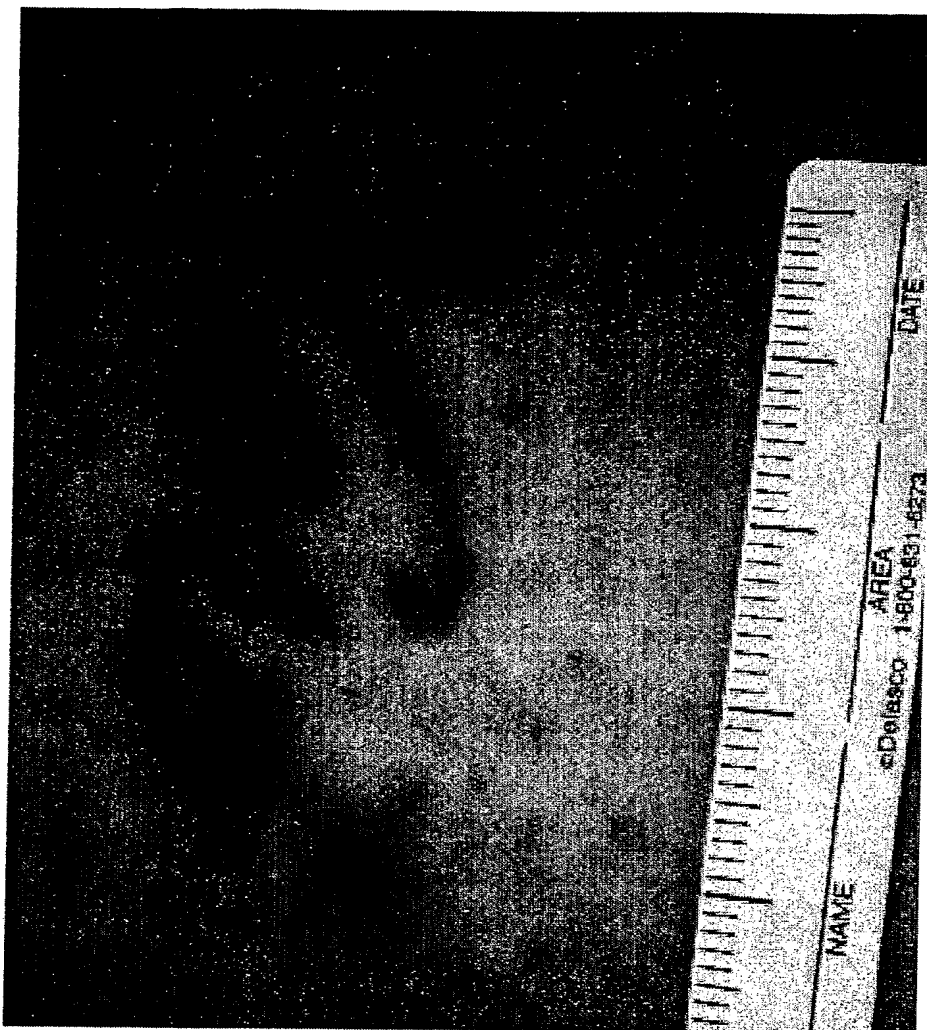


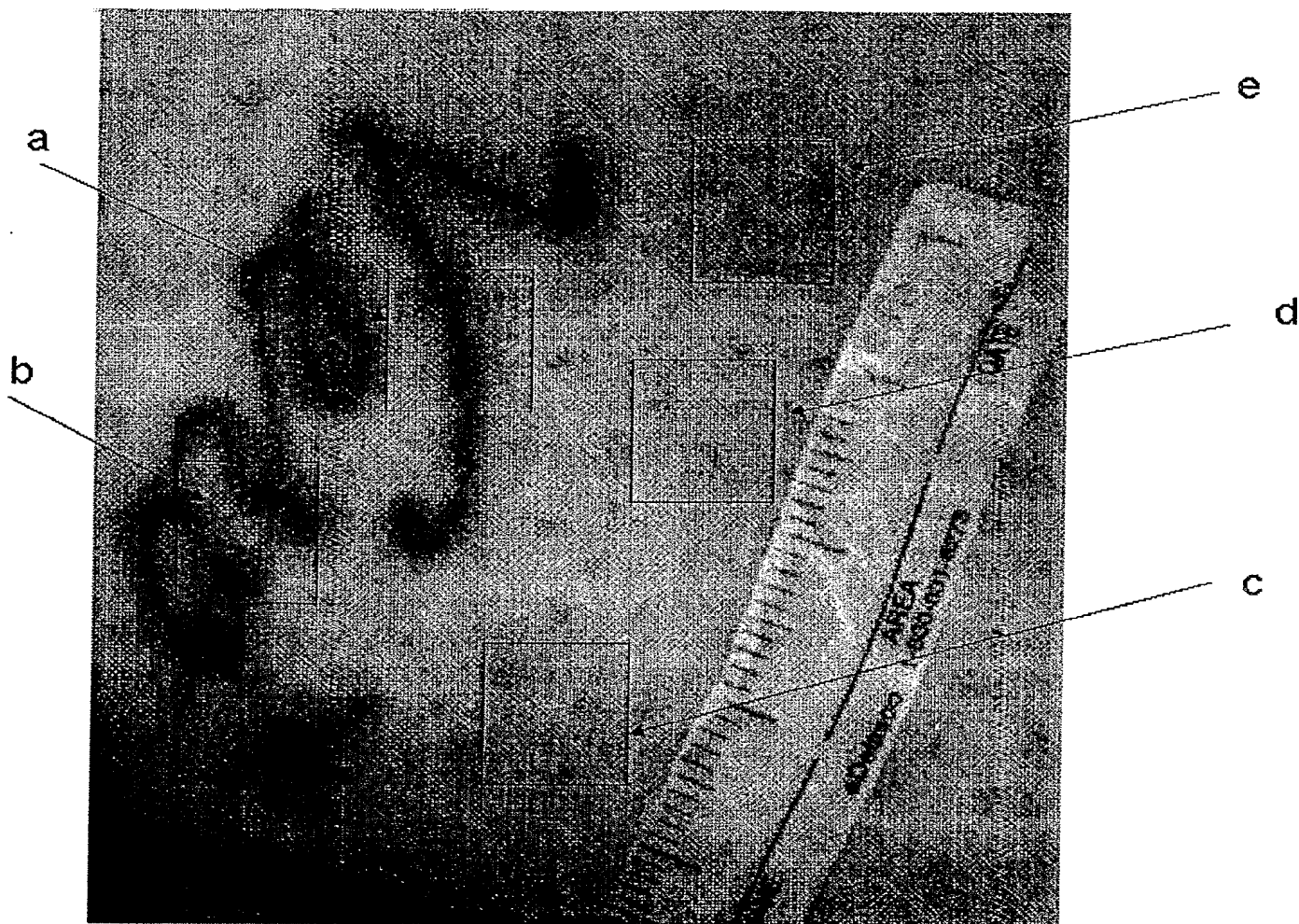
FIG. 56





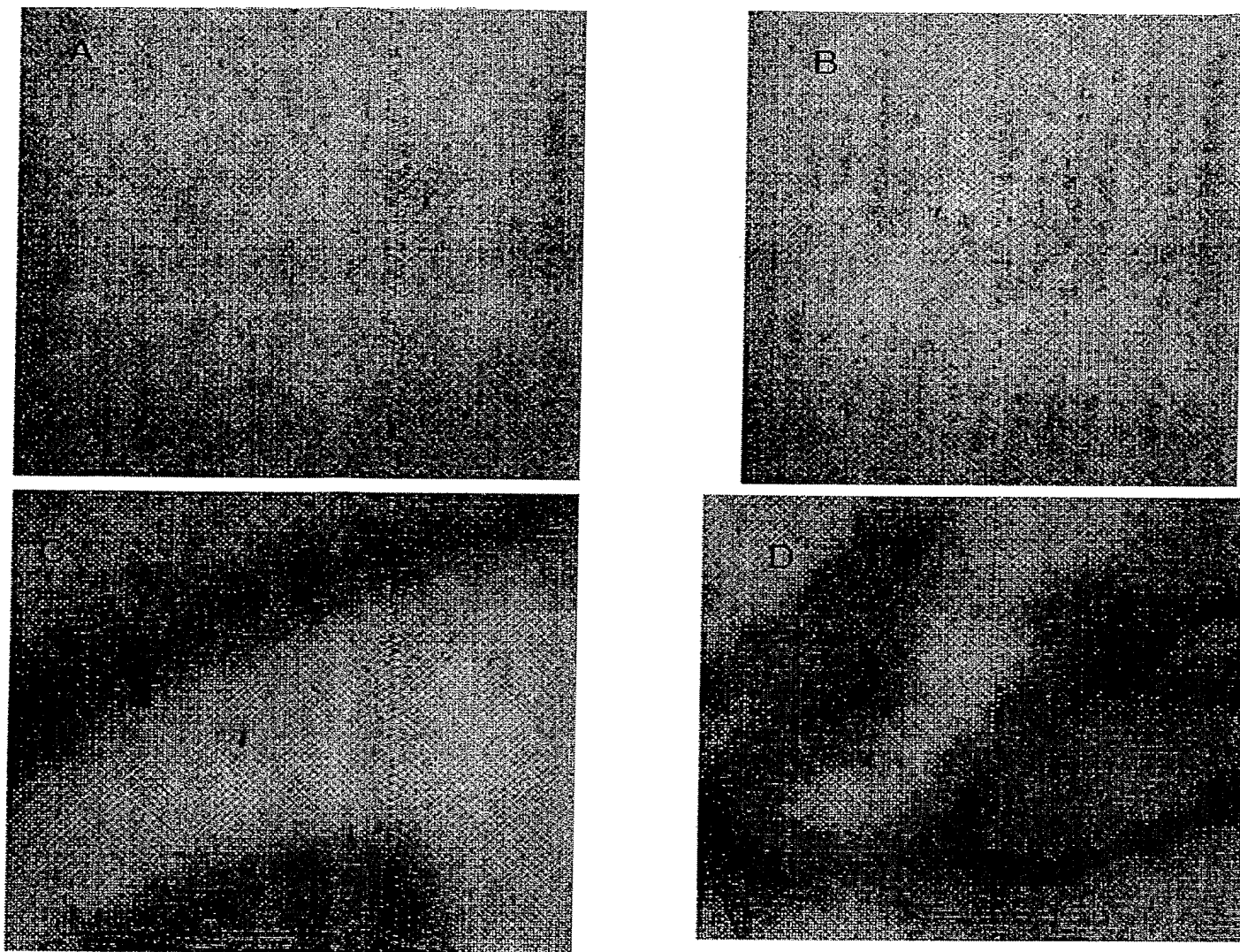
Pre-treatment selected skin area (tattoo on right leg of subject).

FIG. 57



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Figure 90 min post-treatment skin area. Two different tattoo sites of skin were treated with two pulses of  $18 \text{ J/cm}^2$  - 10 ms and  $24 \text{ J/cm}^2$  - 20 ms (a and b accordingly). Three different intact skin sites were treated with two pulses of  $24 \text{ J/cm}^2$  - 20 ms, two pulses of  $30 \text{ J/cm}^2$  - 20 ms and three pulses of  $36 \text{ J/cm}^2$  - 20 ms (c-e accordingly).



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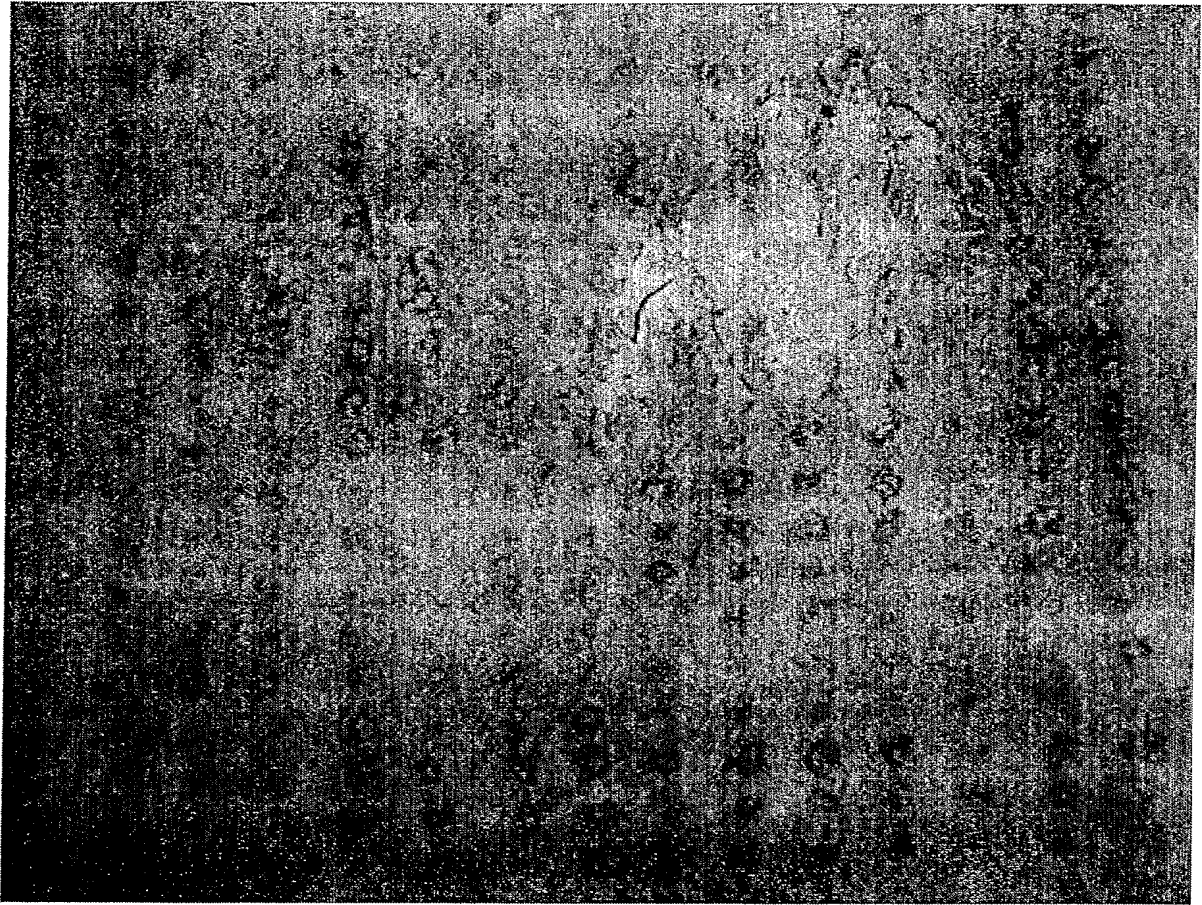
- **Figure** 90 min post-treatment skin area. Notice island damages in the stratum corneum of intact (none-tattooed) skin site of subject after two pulses of  $30 \text{ J/cm}^2 - 20 \text{ ms}$  and three pulses of  $36 \text{ J/cm}^2 - 20 \text{ ms}$  treatment for up to 90 min time points (A and B). Tattooed areas for 90 min time points do not show clearly defined island damages (C and D).



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Figure Island damages for a 24 hour post-treatment tattooed areas are more detectable (compare to Figure ).

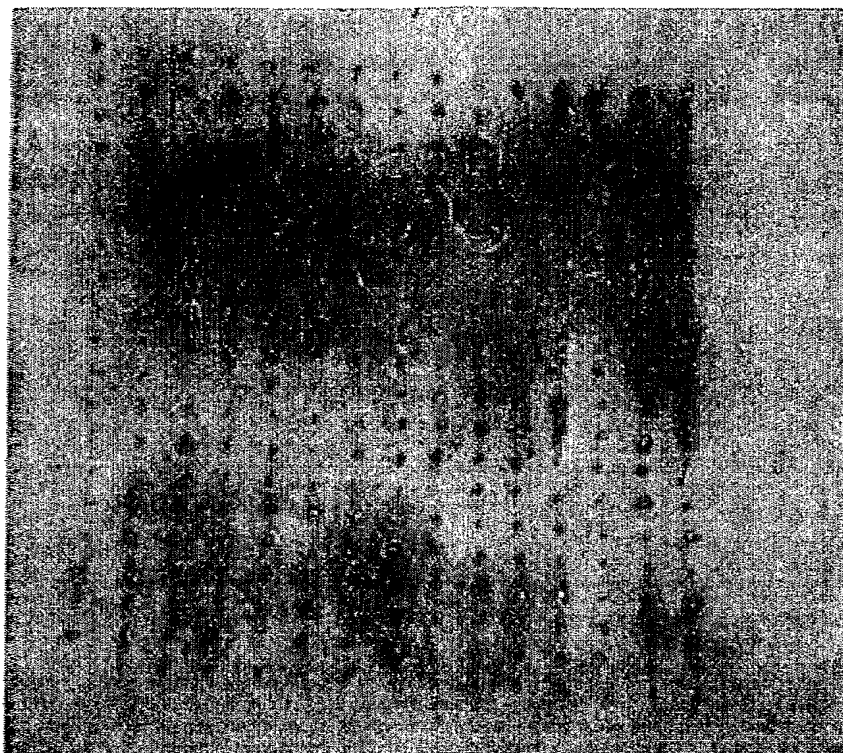
59



9 hour post-treatment skin area. After three pulses of  $36 \text{ J/cm}^2$  - 20 ms treatment the targeted skin site developed edema.

*Fig. 61*





**Figure 62** Area treated with  $36 \text{ J/cm}^2$  - 20 ms and glycerin cream developed redness 48 hrs. post-exposure (compare this Figure to **Figure B5**). The redness is a result of an optical clearance manifesting itself in better visibility of the dermal vasculature.

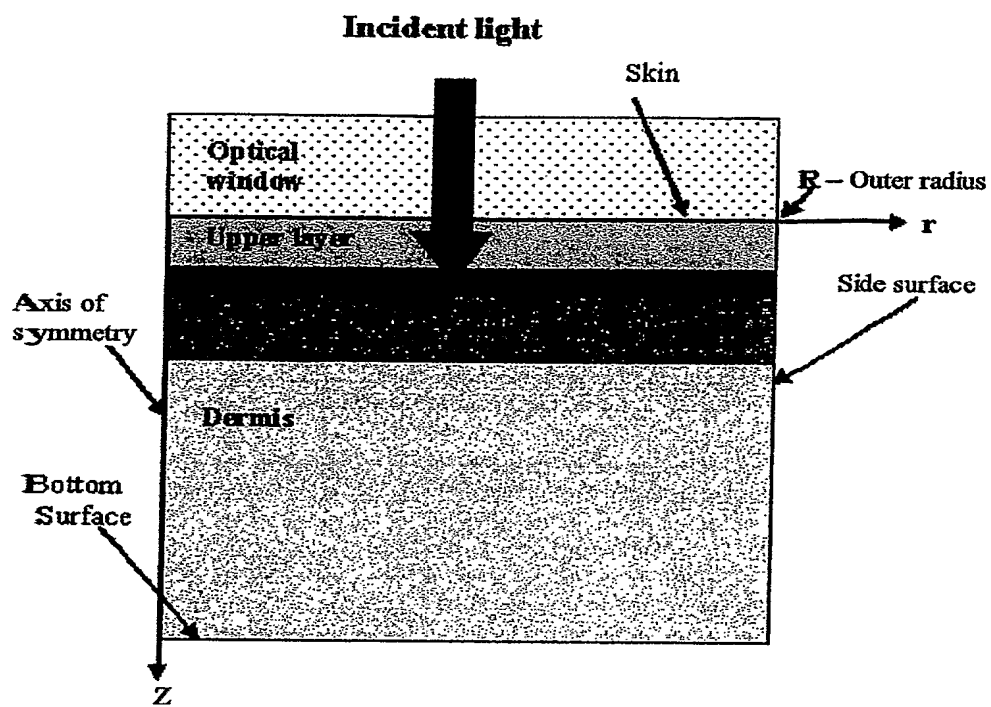


FIG. 63

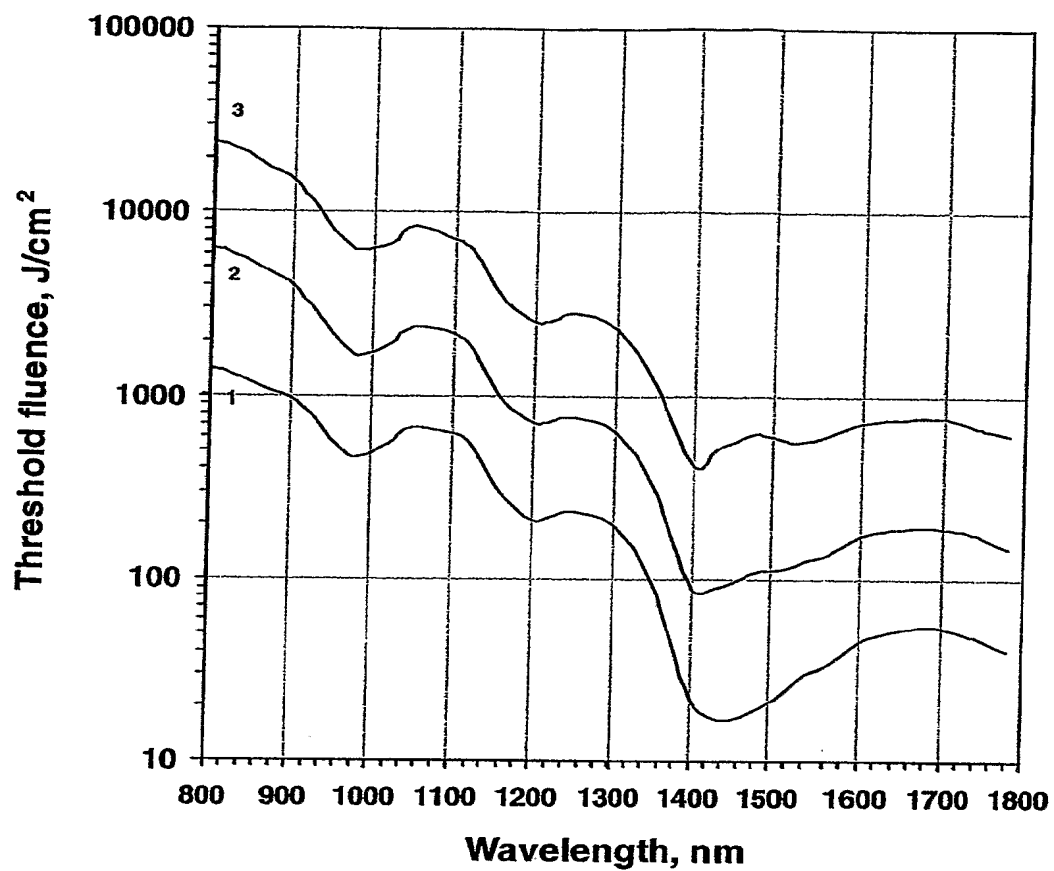


Fig. 64



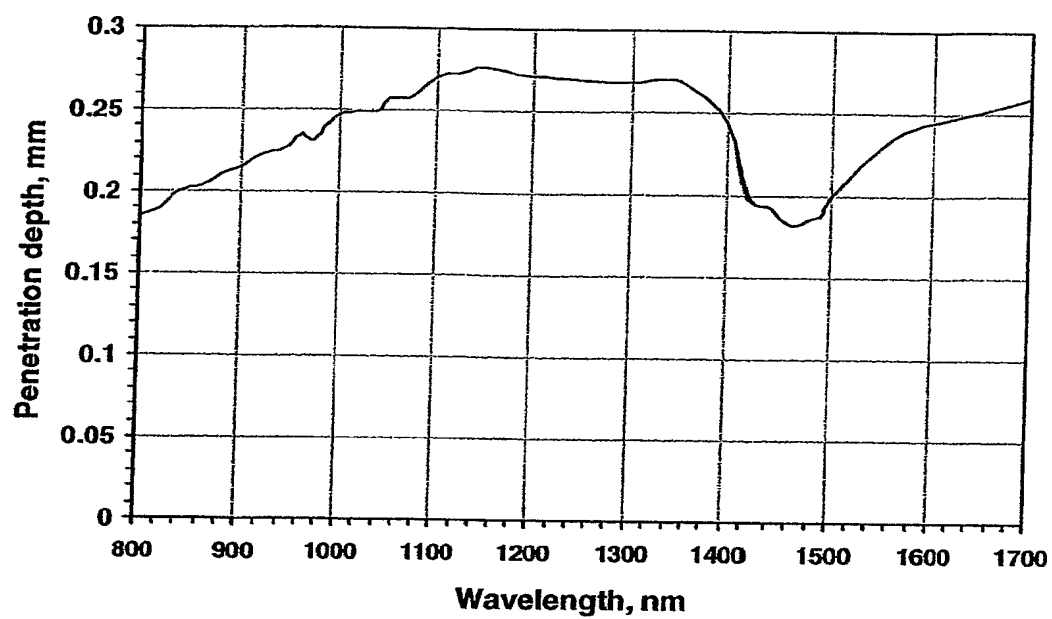


Fig. 65

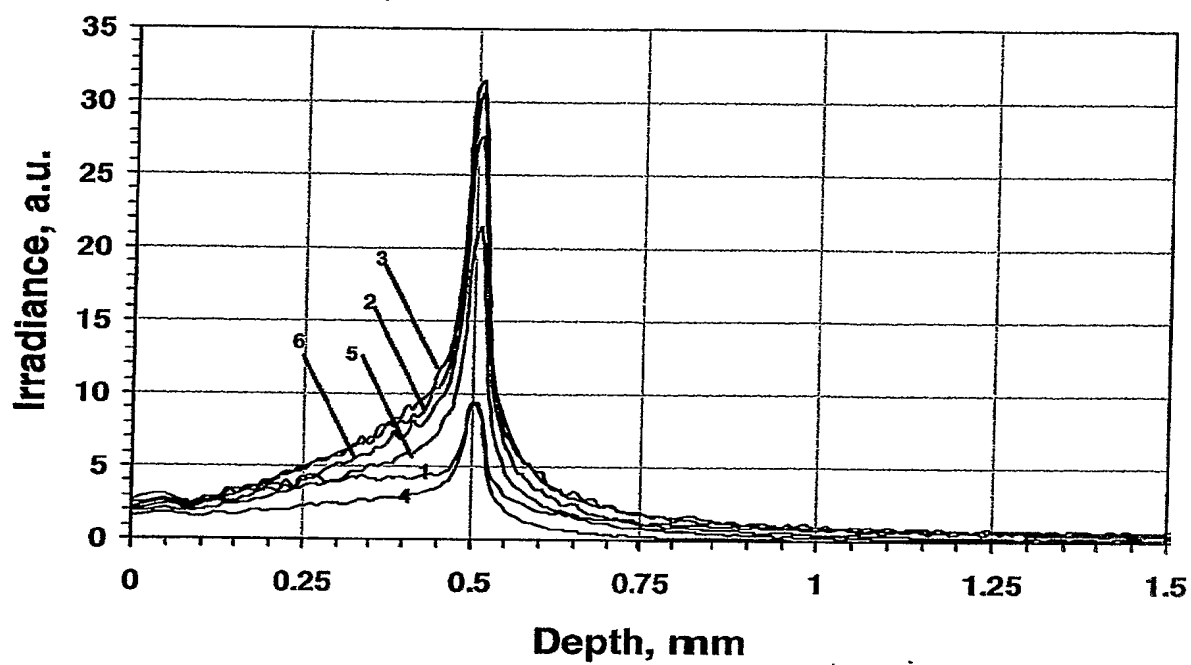


Fig. 66

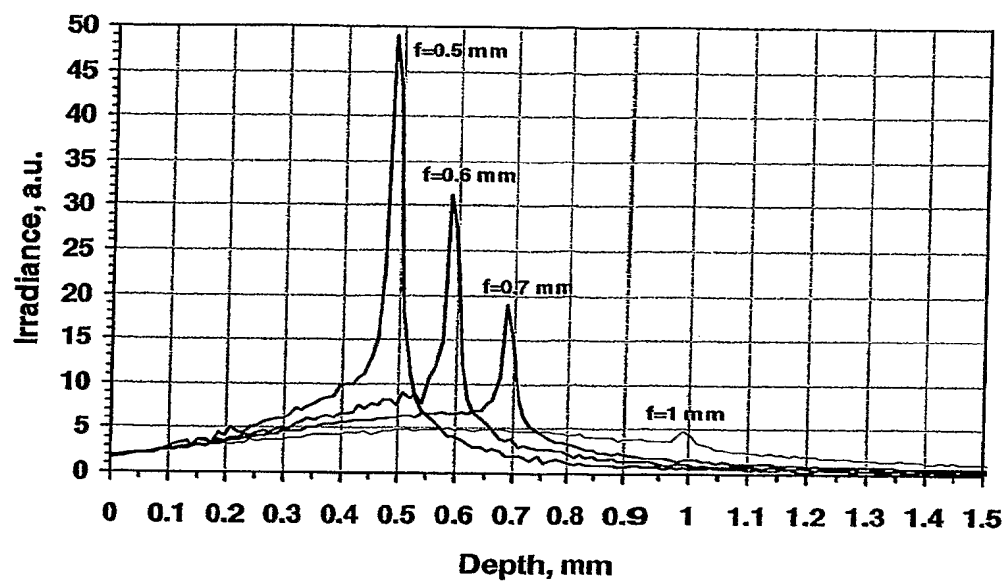


Fig. 67

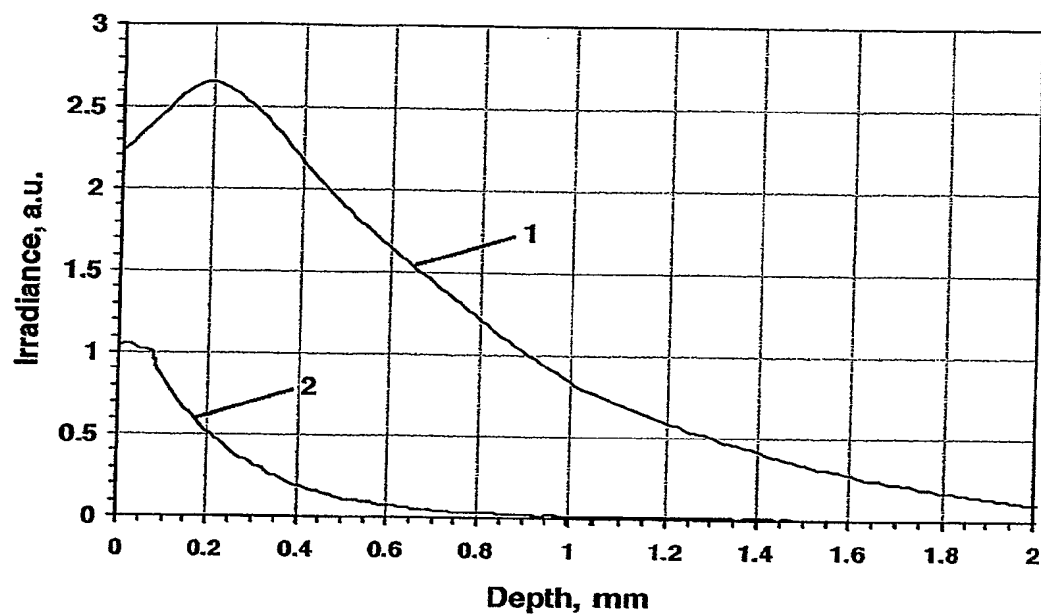


Fig. 68

Table AA1

Layer parameters. The OD values apply to the reference wavelength 800 nm.

| Layer                       | Thickness<br>( $\mu\text{m}$ ) | Refraction<br>index | OD of<br>melanin<br>(skin types<br>I-VI) | Water<br>content,<br>(%) | Blood<br>content,<br>(%) | Mean vessel<br>diameter<br>( $\mu\text{m}$ ) | Scat.<br>coef. at<br>577 nm<br>( $\text{mm}^{-1}$ ) | Density<br>( $\text{g}/\text{cm}^3$ ) | Specific<br>heat,<br>(J/g K) | Thermal<br>conductivity,<br>W/(cm K) |
|-----------------------------|--------------------------------|---------------------|--|--------------------------|--------------------------|--|---|---------------------------------------|------------------------------|--------------------------------------|
| Upper                       | 70                             | 1.45                | I 0.0035                                 | 60                       | 0                        | -  | 30  | 1.12                                  | 3.05                         | 0.00294                              |
|                             |                                |                     | II 0.0061                                |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | III 0.0087                               |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | IV 0.019                                 |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | V 0.0491                                 |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | VI 0.0952                                |                          |                          |  |   |                                       |                              |                                      |
| Basal                       | 15                             | 1.4                 | I 0.0081                                 | 60                       | 0                        | -  | 30  | 1.12                                  | 3.05                         | 0.00294                              |
|                             |                                |                     | II 0.0141                                |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | II 0.0202                                |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | IV 0.0444                                |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | V 0.0491                                 |                          |                          |  |   |                                       |                              |                                      |
|                             |                                |                     | VI 0.0952                                |                          |                          |  |   |                                       |                              |                                      |
| Reticular derm. &<br>plexus | 200                            | 1.38                | 0  | 75                       | 1.7                      | 6  | 12  | 1.075                                 | 3.50                         | 0.00407                              |
| Dermis                      | 3000                           | 1.35                | 0  | 75                       | 1.4                      | 15   | 12  | 1.075                                 | 3.50                         | 0.00407                              |
| Sapphire window             | 3000                           | 1.76                | -  | -                        | -                        | -  | 0   | 3.97                                  | 0.419                        | 0.2721                               |

Table F1

Exemplary treatment parameters.

|  | 1                       | 2                        | 3          | 5         |
|--|-------------------------|--------------------------|------------|-----------|
| Damage heating depth, mm                       |                         |                          |            |           |
| Damage/heated zone diameter, mm                | 0.2 -3                  | 0.5-5                    | 0.75 -6    | 1-10      |
| Wavelength, nm                                 | 900 -1850<br>2080 -2300 | 900 ~ 1400<br>1500 -1750 | 900 - 1350 | 900 -1300 |
| Beam diameter (2D beam) or width (1D beam), mm | 0.5-8                   | 1 - 10                   | 2 - 15     | 3-25      |
| Fill factor*                                   | 0.01-0.5                | 0.01-0.3                 | 0.01 - 0.3 | 0.01-0.3  |
| Pulse width, s                                 | 0.001 - 10              | 0.1- 20                  | 0.5 - 30   | 1-120     |
| Precooling time, s                             | 0 - 10                  | 0 - 20                   | 0 - 60     | 0 -100    |
| Postcooling time, s                            | 0 - 20                  | 0 - 30                   | 0- 60      | 0 - 120   |
| Input power density, W/cm <sup>2</sup>         | 5-100                   | 3- 70                    | 1 - 50     | 0.5 - 35  |

\*F<sub>max</sub> is the maximum possible fill factor, that is, the ratio of the light exposed area to the total area of the treatment site,

$$F = \frac{\pi}{4} \cdot \left(\frac{D}{d}\right)^2$$
, where D is the spot diameter, d is the spot separation.